UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

GILEAD SCIENCES, INC.,

PLAINTIFF, CASE NO. CV-13-4057-BLF

VS. SAN JOSE, CALIFORNIA

MERCK & CO., INC., ET AL., MARCH 10, 2016

DEFENDANTS. VOLUME 5

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TRANSCRIPT OF TRIAL PROCEEDINGS
BEFORE THE HONORABLE BETH LABSON FREEMAN
UNITED STATES DISTRICT JUDGE
A-P-P-E-A-R-A-N-C-E-S

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(APPEARANCES CONTINUED ON THE NEXT PAGE.)

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PROCEEDINGS RECORDED BY MECHANICAL STENOGRAPHY, TRANSCRIPT PRODUCED WITH COMPUTER.

A P P E A R A N C E S: (CONT'D)

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SAN JOSE, CALIFORNIA MARCH 10, 2016

P R O C E E D I N G S

(JURY IN AT 9:03 A.M.)

THE COURT: GOOD MORNING EVERYONE. PLEASE BE SEATED.

WE'RE ON THE RECORD. ALL OF OUR JURORS ARE HERE.

MR. RABINOWITZ: YOUR HONOR, SINCE BOTH OF THE PATENTS ARE IN EVIDENCE, I WAS WONDERING WHETHER THE JURY MEMBERS COULD BE PROVIDED WITH THE HIGHLIGHTED COPIES.

THE COURT: I THOUGHT THEY WERE GIVEN THAT ON THE FIRST DAY OF THE TRIAL.

MR. RABINOWITZ: I DON'T BELIEVE THAT HAPPENED.

THE COURT: THAT'S WHAT I THOUGHT. BUT IT'S BETTER LATE THAN NEVER.

LADIES AND GENTLEMEN, YOU'VE HEARD ABOUT THESE PATENTS AND IT'S MY PRACTICE TO GIVE YOU A COPY OF IT AND HIGHLIGHT THE CLAIMS THAT ARE AT ISSUE. IT'S ONLY BECAUSE THE PRINTS ARE A LITTLE SMALL AND I WANT YOU TO BE ABLE TO SEE THOSE PORTIONS.

OBVIOUSLY THE ENTIRE EXHIBIT IS IMPORTANT, LIKE ALL OTHER EXHIBITS, AND YOU'RE TO USE IT AS YOU DEEM APPROPRIATE.

ALL RIGHT. WE ARE BACK ON THE RECORD AND DR. STELLA HAS RETURNED.

I'M GOING TO HAVE YOU STAND AND BE SWORN FOR A NEW COURT DAY.

(PLAINTIFF'S WITNESS, VALENTINO STELLA, WAS SWORN.)

THE WITNESS: YES.

THE CLERK: THANK YOU.

THE COURT: MR. SINGER, GO AHEAD.

MR. SINGER: THANK YOU, YOUR HONOR.

DIRECT EXAMINATION (RESUMED)

BY MR. SINGER:

Q. GOOD MORNING.

GOOD MORNING TO EVERYONE.

DR. STELLA, WE BROKE AFTER YOU DESCRIBED YOUR BACKGROUND TO THE JURY AND WE QUALIFIED YOU AS AN EXPERT. LET'S GET RIGHT TO THE OPINIONS YOU'VE REACHED.

DR. STELLA, HAVE YOU REACHED ANY OPINIONS ON THE VALIDITY OF THE '499 PATENT IN THIS CASE?

A. YES, I HAVE.

Q. AND HAVE YOU WORKED WITH OUR ART DEPARTMENT TO CREATE A SLIDE PRESENTATION EXPLAINING THOSE OPINIONS SO THAT MAYBE WE CAN GO THROUGH THIS A LITTLE MORE EFFICIENTLY AND SPEEDILY?

A. YES.

Q. ALL RIGHT. LET'S, IF WE COULD, HAVE UP THE FIRST SLIDE OF DR. STELLA.

YOU'VE CHARACTERIZED THIS AS A SUMMARY OF YOUR OPINIONS. IF YOU COULD, FOR THE JURY, DESCRIBE YOUR FIRST BULLET IN THE OPINION.

A. BASICALLY THAT THE CLAIMS COVER A NUMBER OF POTENTIAL PRODRUGS, AND THAT THE COMPOUNDS WITH NO SUPPORTIVE DISCLOSURE,

MEANING THAT THERE'S NO DATA, AND NO PRODRUG EXAMPLES THAT ARE WITHIN THE SCOPE OF THE CLAIMS, THAT MEANS THAT IN THE CLAIM, NONE OF THE COMPOUNDS IN THE CLAIMS OR PRODRUGS IN THE CLAIMS APPEAR IN THE SPECIFICATION.

Q. AND WHAT IS THE CONSEQUENCE OF THAT, IN YOUR OPINION, AS TO THE VALIDITY OF THE ASSERTED CLAIMS OF THE '499 PATENT?

A. WELL, BECAUSE OF THAT I THINK THE CLAIMS ARE NOT -- THEY LACK ENABLEMENT AND IT DOES NOT TEACH ONE HOW TO MAKE AND USE A PRODRUG CLAIMED FOR THE TREATMENT OF HCV.

IT ALSO DOESN'T MEET THE CRITERIA OF WHAT WE CALL WRITTEN DESCRIPTION. IT DOES NOT SHOW THAT THE INVENTORS ACTUALLY INVENTED ANY OF THE PRODRUGS OR THE CLAIMED CLASS OF COMPOUNDS.

Q. OKAY. THE FIRST THING YOU SAY HERE -- AND I'M GOING TO UNDERLINE IT AND WE'LL WIPE IT AWAY -- YOU SAY THAT THE CLAIMS COVER UNLIMITED POTENTIAL PRODRUG COMPOUNDS.

IF WE CAN GO TO THE NEXT SLIDE. THIS IS CLAIM 1 AND WE HAVE ALL SEEN IT BEFORE WITH OTHER WITNESSES.

AND IT'S CALLED A METHOD OF TREATING HEPATITIS C VIRUS INFECTION COMPRISING ADMINISTERING TO A MAMMAL IN NEED OF SUCH TREATMENT A THERAPEUTICALLY EFFECTIVE AMOUNT OF A COMPOUND OF THE MARKUSH STRUCTURE.

DID I READ THAT CORRECTLY?

A. YES.

Q. NOW, DR. STELLA, I DON'T SEE THE WORD "PRODRUG" THERE. I DON'T SEE IT. WHY DO YOU SAY THAT THE CLAIM COVERS UNLIMITED

POTENTIAL PRODRUGS?

A. WELL, THE -- I'VE HIGHLIGHTED THE WORD "ADMINISTERING" HERE. THE COURT HAS CONSTRUED, IN WHAT WE CALL CLAIM CONSTRUCTION, THAT ADMINISTERING MEANS PROVIDING A COMPOUND OF THE INVENTION OR A PRODRUG OF THE COMPOUND OF THE INVENTION TO AN INDIVIDUAL IN NEED.

SO IT'S IN THAT CONSTRUCTION THAT THE WORD PRODRUG -- ADMINISTERING IS WHAT INCLUDES THE PRODRUGS.

Q. SO IF I UNDERSTAND, AND THIS IS NEW FOR THE JURY AND THEY HAVE NOT HEARD THIS BEFORE, THE WORD "ADMINISTERING" HAS A SEPARATE MEANING THAT THE PARTIES ARE TO APPLY IN THIS CASE; IS THAT CORRECT?

A. THAT'S CORRECT.

Q. AND THAT MEANING YOU'VE LISTED ON YOUR PDX-604 AS PROVIDING A COMPOUND OF THE INVENTION OR A PRODRUG OF THE COMPOUND OF THE INVENTION TO THE INDIVIDUAL IN NEED.

WHY DO YOU SAY THAT DEFINITION MEANS THAT THE CLAIM COVERS UNLIMITED POTENTIAL PRODRUGS?

A. BECAUSE IT SAYS ANY PRODRUG. A PRODRUG OF ANY COMPOUND WITHIN THE CLAIM, RIGHT?

Q. IS THE CLAIM LIMITED TO ANY PARTICULAR TYPE OF PRODRUG?

A. NO, NOT AT ALL.

Q. OKAY. IT SIMPLY HAS TO BE A PRODRUG OF ONE OF THE COMPOUNDS COVERED BY THE CLAIMS; IS THAT CORRECT?

A. THAT'S MY UNDERSTANDING, YES.

Q. OKAY. NOW, LET'S STEP BACK -- NOW THAT WE HAVE THE CLAIM AND WHAT IT COVERS, LET'S STEP BACK TO THE REASONS FOR YOUR OPINIONS. ALL RIGHT? CAN WE DO THAT?

A. YES.

Q. FIRST OFF, A LITTLE FORMALITY. WE WENT THROUGH THIS WITH DR. SEEGER. DID YOU, DR. STELLA, ANALYZE THE CLAIMS FROM THE REQUIRED PERSPECTIVE, REQUIRED UNDER PATENT LAW, OF THIS HYPOTHETICAL, MADE UP PERSON OF ORDINARY SKILL IN THE ART, WHICH WE LEARNED IS ACTUALLY KIND OF A TEAM OF PEOPLE, DID YOU DO THAT?

A. THAT'S CORRECT. THAT'S CORRECT.

Q. AND WE HAVE THE DEFINITION IN THE NEXT SLIDE, PDX-605.

THANK YOU, MR. ANG.

FIRST OFF, JUST REAL QUICK, DO YOU QUALIFY AS A -- AS ONE OF THE TEAM MEMBERS OF A PERSON OF ORDINARY SKILL IN THE ART?

A. YES, I THINK I DO.

Q. AND, IN FACT, YOU EXCEED THAT, DON'T YOU?

A. I BELIEVE I DO, YES.

Q. OKAY. NO TIME TO BE HUMBLE HERE TODAY.

SAME QUESTION WE ASKED DR. SEEGER. HOW DO YOU DO THAT? HOW DO YOU, WITH 40 YEARS OF EXPERIENCE IN THIS, PUT YOURSELF IN THE SHOES OF THIS HYPOTHETICAL PERSON OF ORDINARY SKILL IN THE ART?

A. WELL, I DO THAT EVERY DAY, RIGHT? I HAVE GRADUATE STUDENTS AND POST-DOCS -- I WORK WITH STUDENTS, BOTH

UNDERGRADUATE AS WELL AS GRADUATE STUDENTS, AND SO I'M ALWAYS AROUND PEOPLE LIKE THAT AND SO I UNDERSTAND THEM.

HOPEFULLY SOME OF THEM RAISE UP TO THE LEVEL THAT THEY BECOME EXPERTS AT SOME TIME IN THE FUTURE, BUT AT THIS POINT IN THEIR CAREER, THESE PEOPLE THAT WOULD REPRESENT SOMEONE SKILLED IN THE ART.

I ALSO CONSULT FOR MANY DRUG COMPANIES AND I'M CONTINUOUSLY IN CONTACT WITH PEOPLE AT COMPANIES THAT WOULD MEET THE LEVEL OF A PERSON OF SKILL IN THE ART.

SO I THINK I UNDERSTAND AND APPRECIATE A PERSON WITH THAT SKILL SET.

Q. OKAY. NOW, THIS PERSON OF ORDINARY SKILL IN THE ART, THAT'S SOMEONE WHO HAS GOT SOME SKILL, BUT IS NOT AN EXPERT OR INVENTOR; IS THAT CORRECT?

A. THAT'S CORRECT.

Q. OKAY. FAIR ENOUGH.

NOW, I KNOW THE MERCK EXPERT HAD A SLIGHTLY DIFFERENT DEFINITION. HAVE YOU LOOKED AT THAT DEFINITION?

A. YES, I HAVE.

Q. DO YOU ALSO MEET THEIR DEFINITION?

A. YEAH, I MEET THEIR DEFINITION, YES.

Q. AND DO YOUR OPINIONS CHANGE USING THE DEFINITION THAT YOU'VE PROVIDED, OR THE MERCK DEFINITION WHICH I ASSUME THAT WE'LL SEE LATER IN THE TRIAL?

A. IT'S -- IT'S -- TO ME IT'S A VERY SIMILAR -- IT REALLY

DOESN'T CHANGE MY OPINION AT ALL.

Q. OKAY. ALL RIGHT. WITH THAT FORMALITY OUT OF THE WAY, LET'S TALK ABOUT PRODRUGS.

THE JURY HAS HEARD FROM DR. SOFIA ABOUT PRODRUGS, BUT FOR MOST OF THEM IT'S A NEW CONCEPT.

YOU WEREN'T HERE WHEN DR. SOFIA TESTIFIED, BUT HAVE YOU HAD A CHANCE TO REVIEW HIS TESTIMONY?

A. YES, I HAVE. I HAVE READ HIS TRANSCRIPTS.

Q. OKAY. NOW, YOU'RE AN EXPERT IN THE AREA. CAN YOU JUST, FOR THE LADIES AND GENTLEMEN OF THE JURY, AND ALL OF OUR BENEFITS, EXPLAIN AGAIN WHAT A PRODRUG IS IN YOUR EXPERT OPINION?

A. WELL, A PRODRUG IS A MATERIAL -- SO WHEN DRUGS ARE DISCOVERED, EITHER FROM NATURAL SOURCES OR THROUGH MEDICINAL CHEMISTRY PROGRAMS, AND YOU HAVE A DRUG THAT YOU NEED TO DELIVER TO A PATIENT TO AFFECT A DISEASE, SOMETIMES THE PROPERTIES OF THAT DRUG ARE SUCH THAT IT'S REALLY NOT DELIVERABLE OR FORMULATABLE OR DELIVERABLE TO A PATIENT. IT HAS SOME WARTS.

AND AS A RESULT OF THAT, WHAT YOU WANT TO BE ABLE TO DO, AND ONE OF THE WAYS WE ATTACK THAT, IS TO SAY CAN I CHANGE THE STRUCTURE OF THE MOLECULE SO THAT IT OVERCOMES THAT WART.

AND THEN WE DESIGN IT IN SUCH A WAY THAT WHATEVER YOU DO TO CHANGE IT IS CLIPPED OFF AND RELEASES THE DRUG.

SO THE WORD "PRODRUG" IS, IS A GOOD EXAMPLE, THE WORD

"PRODRUG." ACTUALLY THE INVENTOR OF THAT NAME WAS AN AUSTRALIAN, SO I THOUGHT THAT WAS PRETTY COOL.

Q. AND SO YOU HAVE A DEPICTION HERE OF PDX-606. WHAT ARE WE LOOKING AT? WE HAVE PRODRUG AND PROMOIETY. WHAT ARE WE LOOKING AT?

A. THIS IS AN ILLUSTRATION THAT I'VE USED IN A LOT OF MY PAPERS AND SO I REPRODUCED IT HERE FOR THE JURY AND THE TRIAL.

SO IF WE HAVE A DRUG, THAT'S WHAT WE'RE TALKING ABOUT, IT'S A MATERIAL THAT HAS SOME LIMITATION, SOME BARRIER TO ITS UTILITY.

NOW, THAT BARRIER COULD BE SOMETHING AS COMPLEX AS TARGETING THE LIVER TO TREAT HCV.

THAT COULD BE SOMETHING ALSO WHERE, FOR EXAMPLE, THE DRUG MAY TASTE HORRIBLE AND YOU WANT A MASK THE TASTE SO IT CAN BE GIVEN TO CHILDREN.

OR IT MIGHT BE THAT YOU HAVE A DRUG THAT CAN'T BE GIVEN BY INJECTION BECAUSE YOU CAN'T DISSOLVE IT AND BE ABLE TO INJECT IT SAFELY INTO A PATIENT.

SO A PRODRUG IS WHERE YOU TAKE THAT MOLECULE AND YOU IDENTIFY WHAT THE BARRIER OR HURDLE TO THE USE OF THAT DRUG IS AND WE CHEMICALLY CHANGE IT BY PUTTING ON ONE OR MORE PROMOIETIES. I'VE USED THAT TERMINOLOGY AND I'M JUST REPRODUCING IT HERE FOR YOU GUYS, BUT A PROMOIETY IS WHERE WE WOULD ALTER THE CHEMICAL STRUCTURE OF THE MATERIAL TEMPORARILY SO IT CAN OVERCOME THE BARRIER, AND ONCE IT GETS INTO THE BODY

OR PAST THAT BARRIER, WE DESIGN IT SUCH THAT WE HAVE A TRANSFORMATION THAT ESSENTIALLY CUTS OFF, DELETES THE ADDITIONAL PART OF THE MOLECULE AND RELEASES THE DRUG.

SO THIS IS A TECHNOLOGY THAT HAS BEEN FOUND TO BE EFFECTIVE.

Q. JUST GENERALLY SPEAKING, DR. STELLA, DO PEOPLE OF SKILL IN THE ART REGARD THIS AS A SIMPLE TASK OR A CHALLENGING TASK?

A. IT'S A VERY, VERY DIFFICULT TASK AND VERY CHALLENGING AND IT TAKES A LOT OF CREATIVITY TO COME UP WITH PRODRUGS.

AS I SAID YESTERDAY, WHEN I WORKED ON MY PH.D. DISSERTATION, AT THE TIME THAT I WAS WORKING ON PHENYTOIN, FOR EXAMPLE, AND I WAS ONE SKILLED IN THE ART AS A GRADUATE STUDENT TO WHERE I WAS ABLE TO STEP OVER THE LINE AND BECOME THAT CREATIVE INDIVIDUAL THAT LED TO FOSPHENYTOIN, THE DRUG THAT WE TALKED ABOUT YESTERDAY. IT TOOK ME ABOUT TEN YEARS IN THAT CASE.

Q. OKAY. I HAVE A QUESTION KIND OF OUT OF LEFT FIELD HERE, AND IT WILL MAKE SENSE IN A MINUTE. DID YOU RUN TRACK IN HIGH SCHOOL?

A. YES, I DID.

Q. OKAY. DO YOU HAVE AN ANALOGY THAT YOU WOULD LIKE TO SHARE WITH THE JURY ABOUT THE PROCESS OF CREATING A PRODRUG?

A. I WOULD.

AND COULD I HAVE THE NEXT TRANSPARENCY, PLEASE?

Q. IF WE CAN GO TO THE NEXT SLIDE.

A. SO MY UNFAVORITE RACE, BUT ONE I HAD TO RUN BECAUSE I WAS THE ONLY ONE THAT WAS GAME ENOUGH TO DO IT, WAS TO RUN THE 400 METER HURDLE, AND THAT'S A TOUGH RACE. THERE ARE ONLY TWO TOUGHER RACES, WHICH MAY BE THE MARATHON AND STEEPLECHASE.

AND I RAN THE 400 METERS, SO I ALWAYS USED THIS ANALOGY OF HURDLES IN DEVELOPING A DRUG BECAUSE I COULD RELATE TO THE FACT THAT I HAVE TRIPPED OVER A NUMBER OF THESE ALONG THE WAY, BOTH FIGURATIVELY AND ACTUALLY.

SO CAN I GO AHEAD AND, AND EXPLAIN?

Q. CAN I ASK YOU ONE QUESTION BEFORE YOU DO?

A. RIGHT.

Q. IS THIS HURDLE CONCEPT SOMETHING THAT YOU USE IN YOUR TALKS AROUND THE COUNTRY AND AT OTHER COMPANIES?

A. RIGHT. I USUALLY GIVE SHORT COURSES ON PRODRUGS AND SEMINARS AND I DO IT ALL OVER THE COUNTRY.

IN FACT, LAST -- THE MIDDLE OF LAST YEAR I GAVE A ONE DAY SHORT COURSE TO A MEDICINAL CHEMISTRY GROUP AT MERCK.

Q. OKAY. NOW, LET'S TALK ABOUT YOUR DEMONSTRATIVE. YOU START HERE AT THE BEGINNING WITH THE STARTING LINE WITH THE ACTIVE DRUG, WHICH WE SAW, I THINK YOU JUST CALLED IT A DRUG ON YOUR OTHER DEMONSTRATIVE.

WHAT IS IMPORTANT ABOUT THAT STARTING LINE?

A. WELL, I LIKE TO USE THE ANALOGY OF THE 400 METER RACE AT THE OLYMPICS. NOT EVERYBODY GETS TO GET IN THE STARTING BLOCK, RIGHT? YOU HAVE TO BE GOOD TO GET TO THE STARTING BLOCK.

AND SO IN THE ANALOGY TO PRODRUG DEVELOPMENT, YOU HAVE TO HAVE SOMEWHERE -- YOU'VE GOT TO BE ABLE TO STEP INTO THE STARTING BLOCK, AND THAT MEANS THAT YOU HAVE TO IDENTIFY A COMPOUND THAT YOU'RE GOING TO START WITH TO MAKE A PRODRUG OFF TO MAKE IT BETTER, RIGHT? YOU HAVE TO IDENTIFY WHY THERE'S A PROBLEM.

AND SO GETTING TO THE STARTING BLOCK TO ME IS -- YOU CAN'T WIN THE RACE IF YOU CAN'T FIND THE STARTING BLOCKS.

Q. I'M GOING TO ASK YOU A QUESTION ABOUT THAT. IS THERE EVEN A STARTING BLOCK THAT'S WITHIN THE SCOPE OF THE CLAIMS IN THE '499 PATENT?

A. ABSOLUTELY NOT.

Q. ALL RIGHT. LET'S PUT THAT TO ONE SIDE, THAT THERE'S NO STARTING BLOCK.

AND IF YOU CAN TALK ABOUT THE FIRST FEW HURDLES AND EXPLAIN THEM TO THE JURY?

A. RIGHT. WELL, I'VE IDENTIFIED THESE 8 HURDLES, AND BY THE WAY, IT'S NOT LIMITED TO THE 8 HURDLES. THAT'S THE ONLY 8 THAT I COULD FIT ON A PAGE. AND IF YOU'VE EVER RUN THE 400 METER, IT'S ACTUALLY 12 HURDLES TO PUT IT IN PERSPECTIVE.

BUT WHAT I'D LIKE TO DO IS WALK YOU THROUGH KIND OF THE CRITICAL HURDLES IN DEVELOPING A DRUG THAT CAN BE GIVEN ORALLY, OKAY?

SO LET'S ASSUME THAT WE HAVE AN ACTIVE DRUG AND WE'VE IDENTIFIED AN ACTIVE DRUG WHICH IN THE CASE OF THE '499 PATENT

IS NOT THE CASE.

BUT ASSUMING WE HAVE THAT, I'D LIKE TO WALK YOU THROUGH, ESSENTIALLY, THE THOUGHT PROCESS OF HOW YOU WOULD DEVELOP A DRUG THAT EVENTUALLY IS GOING TO BE TARGETED PASSED TO THE LIVER FOR THE TREATMENT OF HEPATITIS C.

SO, FIRST OF ALL, ASSUMING THAT YOU'VE GOT A STARTING A STARTING BLOCK, A BIG ASSUMPTION IN MY MIND, THE FIRST STEP IS THAT YOU'VE GOT TO SYNTHESIZE A PRODRUG. THAT MEANS THAT YOU HAVE TO IDENTIFY A PRODRUG APPROACH OR A SERIES OF PRODRUG APPROACHES THAT YOU FEEL COULD GET YOU TO THE FINISH LINE.

THE FIRST STEP IS CAN I MAKE THE MATERIAL, RIGHT? SYNTHESIS IS NOT A TRIVIAL PROCESS. I THINK YOU'VE PROBABLY ALREADY GOT A SENSE OF THAT FROM OTHER SPEAKERS, BUT THE SYNTHESIS OF COMPOUNDS, THESE COMPLEX CHEMICALS, IS NOT A TRIVIAL TASK. IT'S USUALLY THE PURVIEW OF THE MEDICINAL CHEMIST.

I CAN TELL YOU FROM MY OWN EXPERIENCE THAT I'M A CARD CARRYING CHEMIST, BUT OFTEN COMING UP WITH WHAT WE EVEN CONSIDER MINOR CHANGES CHEMICALLY CAN BE A SIGNIFICANT CHALLENGE.

SO ASSUMING I MAKE IT OVER THE FIRST STEP, WHAT HAPPENS WHEN YOU TAKE A DRUG? WHEN YOU SWALLOW A DRUG? WHEN YOU SWALLOW YOUR TYLENOL OR IBUPROFEN, ONE OF THE FIRST STEPS THAT HAS GOT TO HAPPEN IS THAT THE DRUG HAS GOT TO DISSOLVE IN THE INTESTINAL TRACT. YOU DON'T ABSORB THE SOLID PARTICLES. THE

DRUG HAS GOT TO DISSOLVE. THAT'S CALLED DISSOLUTION, OKAY.

NOW, THINK ABOUT WHAT HAPPENS WHEN YOU SWALLOW A TABLET, THE FIRST ORGAN OTHER THAN THE SALIVA THAT YOU SEE IS INTO THE STOMACH. THE STOMACH HAS A PH OF ABOUT 1. SO LET ME EXPLAIN WHAT PH IS.

PH IS THE MEASURE OF THE ACIDITY. AND YOU ALL HEARD ABOUT ACID REFLUX, RIGHT? ACID REFLUX IS YOUR STOMACH HAS A VERY, VERY STRONG -- IT'S DESIGNED TO BREAK UP FOOD PRODUCTS AND BREAK UP THINGS THAT ARE PART OF YOUR NUTRITION SYSTEM, OKAY.

SO YOUR DRUG HAS GOT TO DISSOLVE AND BE CHEMICALLY STABLE IN A VERY HOSTILE ENVIRONMENT, OKAY?

AND AFTER IT LEAVES THE STOMACH, IT'S GOING TO BE EXPOSED TO PH VALUES AND THAT IS MEASURED AS ACIDITY, AND IT'S GOT TO BE -- AND IT CAN BE QUITE BASIC, PH OF WHAT IS CALLED 8.5. THAT NUMBER DOESN'T HAVE TO BE MEANINGFUL TO YOU.

BUT -- SO THE NEXT STEP IS, CAN THE DRUG DISSOLVE? AND THAT'S NOT PREDICTABLE BECAUSE WHEN YOU SYNTHESIZE ANY ONE COMPOUND, ITS PROPERTIES WILL BE DEPENDENT ON THAT MOLECULE, OKAY?

AND IS IT CHEMICALLY STABLE IN THE GASTROINTESTINAL TRACT? THAT'S THE NEXT BARRIER.

THE THIRD BARRIER I'VE GOT LABELLED HERE IS STABILITY TO SURVIVE THE ENZYME ATTACK IN THE GI TRACT. GI TRACT HERE STANDS FOR GASTROINTESTINAL TRACT.

WHY DO WE HAVE ENZYMES THAT CHEW THINGS UP? WHEN YOU HAD

BREAKFAST THIS MORNING OR SALAD LAST NIGHT, YOU HAD OILS, YOU HAD WHEATS, YOU HAVE WHEAT AND SEEDS AND EVERYTHING ELSE.

SO WHAT THE BODY DOES IS TAKE YOUR FOOD PRODUCTS, DIGEST THEM, AND IN DIGESTING THEM, THEY BREAK IT UP INTO THE AMINO ACIDS, ALL OF THE MINOR COMPONENTS, ALL OF THE, LIKE, THE BALLS THAT MAKE UP THESE COMPLEX MOLECULES, YOU ABSORB THOSE MOLECULES, GET INTO THE BODY AND YOUR BODY REASSEMBLES THEM AND CREATES PROTEINS AND THINGS THAT YOUR BODY NEEDS.

IT'S ALSO A DEFENSE MECHANISM. IF YOU SWALLOW SOMETHING THAT THE BODY RECOGNIZES AS BEING BAD FOR YOU, HOPEFULLY IT CHEWS IT UP SO THAT YOU DON'T GET BAD EFFECTS FROM THE FOOD. ALL RIGHT.

AND WE'VE EVOLVED ENZYMES IN THE GASTROINTESTINAL TRACT TO BREAK UP PRODUCTS BOTH FOR THE SAFETY REASONS, AS WELL AS FOR FOOD AND NUTRITIONAL REASONS.

SO IF YOU HAVE A PRODRUG AND YOU WANT IT TO EVENTUALLY GET ACROSS THE FINISH LINE AND IF IT GETS CHEWED UP BY THOSE ENZYMES THAT ARE IN THE INTESTINAL TRACT, YOU'VE LOST ALREADY. YOU'VE TRIPPED OVER THE HURDLE.

IF YOUR PRODRUG HAS TO BE INTACT TO GET TO THE TARGET SITE AND IT GETS CHEWED UP IN A GASTROINTESTINAL TRACT, DESIGNING THAT TO HIT THAT BALANCE OF ENOUGH STABILITY IN THE GI TRACT AND YET GET TO SOME TARGET TISSUE AND WORK IS A REALLY, REALLY, REALLY MAJOR, MAJOR CHALLENGE AND IT'S PROBABLY ONE OF THE TOUGHEST THINGS WE HAVE TO DO.

THE FOURTH THING WE HAVE TO DO IS LET'S ASSUME THE DRUG DOES SURVIVE AND YOU'VE DONE THE GREAT JOB OF DESIGNING YOUR MOLECULE TO DO THAT.

IT THEN HAS TO BE ABSORBED INTO THE BODY. NOW, THE CELLS THAT LINE THE SMALL INTESTINE ARE CALLED ENTEROCYTES. THESE ARE ONE LAYER CELLS THAT ARE ON THE SURFACE OF YOUR INTESTINE AND TO GO ACROSS AND INTO THOSE CELLS TO BE ABLE TO GET INTO THE BLOODSTREAM REQUIRES THE DRUG TO HAVE WHAT WE CALL PERMEABILITY CHARACTERISTICS.

PERMEABILITY IS A FANCY NAME OF BEING ABLE TO CROSS A MEMBRANE, OKAY.

TO CROSS THAT MEMBRANE, IT REQUIRES THE DRUG TO HAVE A BALANCE OF PROPERTIES, AND THAT'S A VERY COMPLEX PROCESS AND I DON'T WANT TO GO INTO A LOT OF DETAILS BECAUSE WE CAN SPEND TOO MUCH TIME ON THAT.

BUT THE BODY HAS WAYS OF PROTECTING ITSELF, AND IT PROTECTS ITSELF BY HAVING IMBEDDED IN THOSE MEMBRANES MOLECULES CALLED E-FLEX PUMPS. THESE ARE THINGS THAT TEND TO PUMP CRAP OUT, OKAY?

IN OTHER WORDS, THE REASON YOU DON'T GET SICK ON SOME OCCASIONS IS BECAUSE THE DRUG YOU TAKE IS AN E-FLEX CANDIDATE AND IT DOESN'T GET INTO THE CELLS.

SO A GOOD EXAMPLE OF THAT, I THINK YOU MAY HAVE HEARD OF THE DRUG IMODIUM, IT IS A DRUG TO TREAT DIARRHEA, RIGHT. IMODIUM WORKS IN THE INTESTINE TO STOP DIARRHEA BECAUSE IT

CAN'T GET INTO THE CELLS IN THE BODY.

IF YOU CAN ACTUALLY GET IMODIUM INTO THE BODY AND INTO THE BRAIN. IT'S ACTUALLY A VERY, VERY STRONG NARCOTIC. BUT IT DOESN'T HAVE NARCOTIC PROPERTIES BECAUSE IT GETS PUMPED OUT, IT'S RECOGNIZED BY THIS E-FLEX AND PUMPS IT OUT.

OKAY. THAT'S WHY IT'S EFFECTIVE TO TREAT DIARRHEA AND IT DOESN'T GIVE YOU HALLUCINATIONS.

Q. DR. STELLA, IF YOU COULD TELL US, WHERE ARE WE ON YOUR HURDLES TO THE FINISH LINE AT THIS POINT?

A. AT 5. SO THAT WAS 4.

AT 5 IT WAS ENZYMES INTO THE ENTEROCYTES THAT ARE RESPONSIBLE FOR FURTHER DESTROYING MATERIALS THAT SURVIVE THE GASTROINTESTINAL TRACT. THE ENTEROCYTES ARE VERY RICH IN ENZYMES FOR DESTROYING MOLECULES, BOTH FOOD PRODUCTS AS WELL AS DRUG MOLECULES.

THE NEXT STEP IS PASSAGE THROUGH THE ENTEROCYTES OF THE OTHER SIDE, IF YOU WOULD LIKE, IT'S CALLED THE BASEMENT MEMBRANE, AND THAT PROCESS HAS MANY OF THE SAME COMPLEXITIES AS BEING TAKEN OUT INTO THE CELLS.

FINALLY, WHEN YOU ABSORB FOOD AND A DRUG PRODUCT AND TAKE YOUR TYLENOL, IT GETS INTO WHAT IS CALLED A PORTAL DRUG SUPPLY SO ALL OF THE BLOOD THAT FEEDS INTO THE INTESTINAL TRACT PICKS UP THE ALL OF THE BLOOD SUPPLY AND GOES TO THE LIVER.

THE LIVER IS YOUR ORGAN -- THE INTESTINAL TRACT IS YOUR OTHER BIG ORGAN THAT SAVES YOU FROM BEING EXPOSED TO THINGS

THAT YOU SHOULDN'T GET EXPOSED TO. BASICALLY IT'S THERE TO CLEAR OUT UNDESIRABLE MOLECULES THAT YOU HAVE EATEN AS PART OF YOUR FOOD DIGESTION PROCESS. SO IT PICKS UP THE BLOOD AND TAKES IT TO THE LIVER.

SO IN THIS PARTICULAR CASE, WE HAVE AN INTERESTING ASPECT OF THIS CASE, OF THIS TYPE OF DRUG. YOU WANT THE DRUG TO ACT IN THE LIVER, OKAY?

SO LET'S TALK A LITTLE BIT ABOUT WHAT THE LIVER IS. THE LIVER CONTAINS MANY CELLS AND YOU CAN THINK OF IT AS A CHEMICAL REACTOR, OKAY?

AND SO IF YOU HAVE A MOLECULE GOING INTO THE LIVER ON ONE SIDE AND YOU WANT IT TO ACT IN THE LIVER, IT ACTUALLY HAS TO BE PICKED UP IN THE LIVER FASTER THAN IT GOES THROUGH THE LIVER.

SO IF IT ACTUALLY GOES THROUGH THE LIVER UNTOUCHED AND ENDS UP ON THE OTHER SIDE OF THE LIVER AND IT GETS DILUTED OUT, THEN YOU HAVE A LESS EFFECTIVE DRUG.

SO IN THIS CASE YOU ALSO HAVE TO DESIGN INTO THE MOLECULE THOSE PROPERTIES THAT ALLOW IT TO BE TAKEN UP BY THE LIVER CELLS.

AND THEN THE REALLY, THE REALLY BIG TASK IN THIS PARTICULAR CASE IS IF YOU'RE TARGETING THE LIVER AND YOU'RE TARGETING A VIRUS IN THE LIVER, YOU HAVE TO DESIGN THAT MOLECULE SUCH THAT IT WILL BREAK DOWN IN THE LIVER INFECTED CELLS, OKAY?

AND THAT -- BOY, SO THAT'S WHAT WE CALL TARGETING OR AN

ASPECT OF TARGETING AND THAT'S A TRULY MAJOR CHALLENGE. YOU CAN PROBABLY COUNT ON A COUPLE OF HANDS THOSE SUCCESSFUL DRUGS THAT HAVE ACTUALLY ACHIEVED SOME GOALS LIKE THAT.

THAT IS THE SORT OF, IN A NUTSHELL, EIGHT BARRIERS. AS I SAID, THERE'S A LOT OF OTHERS.

BUT I LIKE TO -- ONE OF THE WORST RACES I EVER RAN WAS I MANAGED TO GET OVER THE 12TH HURDLE AND PULL THE HAMSTRING ON THE STRAIGHT. SO I DIDN'T MAKE IT.

I MADE IT TO THE FINISH LINE, BUT LET'S SAY I WASN'T HEALTHY WHEN I CROSSED THE FINISHED LINE.

SO YOU CAN DO ALL OF THESE DESIGN ASPECTS, BUT AT THE END OF THE DAY YOU CAN GET TRIPPED UP, RIGHT?

Q. DR. STELLA, THESE HURDLES THAT YOU HAVE JUST DESCRIBED, ARE THOSE SOMETHING THAT A PERSON OF ORDINARY SKILL IN THE ART WOULD HAVE UNDERSTOOD EXISTED BACK IN OUR HYPOTHETICAL TIMEFRAME OF 2002 WHEN THE APPLICANTS FOR PATENT AT MERCK APPLIED FOR THE '499 PATENT?

A. I THINK A PERSON OF SKILL IN THE ART, READING THE LITERATURE, WOULD UNDERSTAND THAT THE DESIGN OF ORAL PRODRUGS IS EXTREMELY CHALLENGING AND THAT THESE BARRIERS CAN CREATE PROBLEMS WITH DESIGN AND IMPLEMENTATION.

Q. NOW, IT'S 2016. WE ALL KNOW THAT.

DO WE KNOW MORE TODAY OR DID WE KNOW LESS BACK IN 2002?

A. WE KNEW A LOT LESS.

Q. OKAY.

A. WE'VE BEEN MORE APPRECIATIVE TODAY AND WE CAN UNDERSTAND THIS A LITTLE BIT BETTER TODAY.

Q. OKAY. NOW, YOUR SLIDE TALKS ABOUT ORAL PRODRUGS. ARE THERE OTHER TYPES OF DELIVERY POSSIBLE AS WELL?

A. YES. I DID ORAL PRODRUGS BECAUSE THAT IS THE PRINCIPAL ROUTE THAT WE PREFER BECAUSE IT'S CONVENIENT FOR THE PATIENT TO TAKE ONE TABLET ONCE A DAY OR ONE TABLET A COUPLE TIMES A DAY. THAT'S A CONVENIENT METHOD FOR TREATMENT.

THERE ARE OTHER ROUTES OF ADMINISTRATION, SUCH AS INJECTIONS OR NASAL SPRAYS AND THINGS LIKE THAT, YES.

Q. OKAY. AND ARE THERE THE SAME HURDLES, DIFFERENT HURDLES, MORE OR LESS?

A. THE HURDLES -- MANY HURDLES ARE VERY SIMILAR, BUT THERE ARE OTHERS AS WELL. SO, FOR EXAMPLE, IN AN INTRAVENOUS INJECTION, NUMBER ONE, YOU'RE PUNCHING THE SKIN AND POTENTIALLY CAUSING A PROBLEM WITH INFECTIONS. EVERY TIME YOU PUNCH THE SKIN YOU HAVE THAT CAPABILITY. SO IT'S NOT THE MOST SAFEST ROUTE OF ADMINISTRATION.

PLUS, IF YOU HAVE TO GIVE AN INJECTION ONCE A DAY FOR EVEN 12 WEEKS, THAT'S NOT SOMETHING THAT IS OBVIOUSLY ENCOURAGED TO DO. BUT IN SOME CASES WE MAY HAVE TO, BUT THAT'S NOT SOMETHING THAT WE TRY TO DO.

PLUS THE PROPERTIES THAT YOU WOULD HAVE TO BUILD INTO YOUR PRODRUG TO BE ABLE TO GIVE A DRUG BY INJECTION, FOR EXAMPLE, REQUIRES A DRUG TO BE IN SOLUTION. DIFFERENT PROPERTY THAN

WHAT YOU'RE TRYING TO DO WITH ORAL.

YOU ALSO HAVE TO DO IT IN A WAY THAT YOU CAN STERILIZE THE PRODUCT. YOU CAN'T INJECT INTO THE PATIENT NONSTERILE PRODUCT. THAT REQUIRES EXPOSING THE DRUG TO SOME STERILIZATION. AND SO THERE NEEDS TO BE PRODUCT DESIGN PROGRAMS THAT ARE TAILORED TO THAT PARTICULAR ROUTE OF ADMINISTRATION.

SO IN TERMS OF THE COMPLEXITY OF THE PRODRUGS, IT'S A DIFFERENT TYPE OF COMPLEXITY. BUT AT THE END OF THE DAY, ALL OF THEM REQUIRE OVERCOMING MAJOR HURDLES.

Q. THANK YOU, DR. STELLA.

ONE MORE QUESTION ABOUT THIS. IF YOU ARE LUCKY ENOUGH TO FIGURE OUT A PRODRUG STRATEGY FOR ONE ACTIVE, WILL THAT SAME STRATEGY WORK FOR A DIFFERENT ACTIVE, EVEN ONE IN THE SAME CLASS?

A. NO, NOT NECESSARILY.

AND I LIKE TO USE AN ANALOGY, IF YOU DON'T MIND. EXCUSE ME.

I'VE GOT TWO KEYS HERE, RIGHT? ONE OF THEM OPENS -- THIS ONE OPENS MY OFFICE DOOR, THIS ONE OPENS THE FRONT DOOR OF MY BUILDING (INDICATING).

IF I MATCH THEM UP TOGETHER, IF YOU LOOK AT THIS -- AND I CAN'T SHOW YOU PERSONALLY HERE -- BUT ALL THE TEETH MATCH UP EXCEPT FOR ONE, ONE LITTLE TOOTH.

THAT'S THE ANALOGY OF A SMALL DIFFERENCE IN A DRUG MOLECULE.

ONE OPENS MY FRONT DOOR AND ONE OPENS MY OFFICE DOOR, BUT THEY DON'T WORK ON THE OTHERS.

SO VERY SMALL DIFFERENCES CAN MAKE VERY SMALL DIFFERENCES IN DRUG MOLECULES, JUST AS THERE ARE SMALL DIFFERENCES IN KEYS, CAN HAVE A TREMENDOUS EFFECT ON DRUG DEVELOPMENT.

I ALSO LIKE THE ANALOGY, THOSE TEETH ARE USELESS. THOSE TEETH ARE USELESS BECAUSE IF I JUST HAD THE TEETH AND THREW IT IN THERE, GUESS WHAT HAPPENS? I CAN'T TURN THE LOCK. RIGHT?

IT'S THE REST OF THE MOLECULES, THE HANDLE IF YOU WOULD LIKE. IT MAY SEEM TO BE IRRELEVANT, BUT THAT KEY DOESN'T WORK WITHOUT THE HANDLE.

SO IF YOU THINK ABOUT THIS PROCESS, IT'S A VERY SIGNIFICANT CHALLENGE.

Q. AND WAS THAT TRUE FOR NUCLEOTIDES AND NUCLEOSIDES BACK IN 2002?

A. YES.

Q. AND LET'S GO BACK TO YOUR OPINIONS, AND IF WE GO TO THE NEXT SLIDE WITH THAT CLAIM, THE WORD "ADMINISTERING" IS HIGHLIGHTED THAT WAS CONSTRUED TO COVER ANY PRODRUG.

FIRST OFF, WE HAVE THIS PENTAGON, THE FIVE-SIDED FIGURE, AND WE HEARD THAT'S CALLED A MARKUSH STRUCTURE. DO YOU AGREE THAT THIS IS A MARKUSH STRUCTURE?

A. THAT'S MY UNDERSTANDING.

Q. SO THAT MEANS, IF I'VE GOT IT RIGHT, THAT YOU CAN SUBSTITUTE AT THESE VARIOUS POINTS R2, R3, R1, R5, R6 DIFFERENT

THINGS THAT ARE LISTED IN THE CLAIMS; IS THAT CORRECT?

A. AND Y.

Q. OH, THERE'S ANOTHER ONE. SORRY.

THAT THE CLAIM THEN DEFINES THESE WITH DIFFERENT POSSIBLE SUBSTITUENTS; IS THAT CORRECT?

A. THAT'S CORRECT.

Q. NOW, IF IT GOES -- AS FAR AS PRODRUGS ARE CONCERNED, DOES THE PRODRUG APPROACH, I TAKE IT, THEN DEPENDS ON WHAT SUBSTITUENT THERE IS; IS THAT RIGHT?

A. THAT'S CORRECT.

Q. NOW, LOOKING AT THE MARKUSH STRUCTURE AND THE BASE, AND THE BASE IS DOWN HERE, WHERE WOULD A PERSON OF SKILL IN THE ART THINK OF POSSIBLY PUTTING A PRODRUG MOIETY THAT, THAT LITTLE -- NOT LITTLE -- BUT THE MOIETY YOU DESCRIBED, WHERE COULD A PERSON OF SKILL IN THE ART PUT A PRODRUG MOIETY ON THE MARKUSH STRUCTURE AND/OR THE BASE?

A. WELL, IN THE WAY -- WELL, IN COMING TO THAT ANALYSIS, A PERSON OF SKILL IN THE ART WOULD LOOK AT NOT ONLY THE MARKUSH STRUCTURE, BUT ALSO LOOK AT WHAT ARE THE LIMITS WITHIN THAT MARKUSH STRUCTURE.

SO, FOR EXAMPLE, R3 HERE, IF I CAN FIND IT.

Q. IT'S RIGHT HERE (INDICATING).

A. R3 IS A HYDROXYL ALKOXY OR A FLUID, RIGHT?

SO, FOR EXAMPLE, IN THE CASE OF A HYDROXYL COMPOUND, WHICH WOULD BE R3, THAT MEANS YOU COULD PUT A LOT, HUNDREDS IF NOT

THOUSANDS, OF POSSIBLE SUBSTITUENTS ON THERE THAT COULD BE USED TO AFFECT DELIVERY OF THE DRUG.

Q. AND THAT WOULD BE A PRODRUG?

A. THAT WOULD BE A PRODRUG.

Q. ARE THERE OTHER SPOTS THAT YOU COULD PUT THE PRODRUG?

A. R1 IS -- CAN ALSO BE -- NO.

ACTUALLY, R1 IS PROBABLY -- THE WAY IT'S DEFINED HERE IS PROBABLY NOT A FUNCTION OR AN AREA THAT COULD BE DERIVED, ALTHOUGH IT'S POSSIBLE, OKAY.

R3 IS AGAIN A HYDROXYL -- I'M SORRY. I SAID R3.

R2 CAN BE A HYDROXYL, AND SO THAT'S ANOTHER SIDE IN WHICH THERE COULD BE, IN FACT, PRODRUGS ATTACHED.

Y, THAT'S VERY, VERY COMPLEX AREA. IF YOU KNOW Y HERE CAN BE A HYDROXYL AND IT CAN BE AN ALKOXY, IT CAN BE A PHOSPHATE, TRIPHOSPHATE, MONOPHOSPHATE.

AND THEN WITHIN THE PHOSPHATE YOU'VE GOT R9 AND R10 WHICH ARE ALSO MULTIPLE SUBSTITUENTS.

SO THESE WOULD BE THREE AREAS IN WHICH YOU COULD GET ADDITIONS, AND THEN YOU'VE GOT THE BASE.

IN THE CASE OF THE BASE, THE WAY THIS IS WRITTEN --

CAN I CLEAR THIS?

Q. I WILL CLEAR IT FOR YOU.

A. OKAY. AND IT SAYS UNDO UP HERE. WOULD THAT WORK FOR ME?

Q. CLEAR ALL IS IN THE BOTTOM LEFT.

A. OKAY. GREAT. THANK YOU.

Q. THE BOTTOM LEFT.

A. AND IF I LOOK AT THE BASE, W HERE COULD BE AN OXYGEN OR SULPHUR. THAT'S THE O AND THE S.

AND BECAUSE OF THAT O AND THE S, IT CAN ENOLIZE. E-N-O-L-I-Z-E.

Q. THE O OR THE S CAN.

A. AND THAT ALLOWS YOU TO ACTUALLY PUT PRODRUGS ON THAT PARTICULAR GROUP.

YOU ALSO HAVE R6, AND R6 CAN BE A FUNCTIONAL GROUP. MANY OF THESE WOULD BE IN THE SUBCATEGORY AND DIRECTLY DERIVATIZABLE FROM A PRODRUG POINT OF VIEW.

THE ONLY FUNCTIONAL GROUP THAT I SAW THAT I THOUGHT YOU COULD -- COULD YOU CLEAR THAT, JON, MR. SINGER? IT SHOULDN'T BE FAMILIARITY, RIGHT.

Q. THAT'S OKAY.

A. AND R5, AND THE WAY R5 IS DESIGNED, I DON'T THINK THAT WOULD BE A FUNCTIONAL GROUP THAT YOU COULD DERIVATIZE, AND SO I DON'T SEE ANY PRODRUGS THAT YOU COULD PROBABLY DO OFF THAT. AT LEAST A PERSON OF SKILL IN THE ART WOULD QUESTION WHETHER YOU COULD DO SOMETHING ON THE R5.

SO, IN OTHER WORDS, THERE'S MULTIPLE SITES, AND MULTIPLE SITES IN THE MOLECULE AND A COMPLEXITY AND PLETHORA OF PRODRUGS THAT ARE POSSIBLE.

Q. AND COULD YOU EVEN GIVE -- COULD YOU EVEN GIVE TO THE LADIES AND GENTLEMEN OF THE JURY A BALLPARK ESTIMATE ABOUT HOW

MANY POTENTIAL PRODRUGS THIS, THIS MEANS THE CLAIM COVERS?

A. WELL, I THINK I USED THE WORD "UNLIMITED" IN MY EXPERT REPORT AND I THINK I WOULD STICK WITH THAT. I DON'T KNOW THAT I COULD PUT A NUMBER, BUT IT WOULD BE IN EXCESS OF A MILLION.

Q. ALL RIGHT. DOES THIS -- DOES THIS RAISE AN ENABLEMENT PROBLEM IN YOUR EXPERT OPINION?

A. I THINK THEY HAVE AN ENABLEMENT PROBLEM, YES.

Q. AND DOES IT RAISE A WRITTEN DESCRIPTION PROBLEM IN YOUR OPINION?

A. ABSOLUTELY.

Q. AND LET'S TURN TO YOUR ENABLEMENT OPINION AND WALK THROUGH THAT.

WE HAVE ON THE NEXT SLIDE A SUMMARY OF A BELIEVABLE STANDARD FOR ENABLEMENT. AND IT SAYS THAT THE PATENT DISCLOSURE MUST ALLOW A PERSON OF SKILL IN THE ART TO PRACTICE THE FULL SCOPE OF THE CLAIMED INVENTION WITHOUT UNDUE EXPERIMENTATION.

WE HEARD ABOUT THIS CONCEPT OF UNDUE EXPERIMENTATION YESTERDAY. WHAT FACTORS DID YOU CONSIDER, DR. STELLA, IN TRYING TO DECIDE WHETHER THE CLAIM REQUIRED UNDUE EXPERIMENTATION AND THUS VIOLATED THE ENABLEMENT STANDARD?

A. WELL, I'VE LISTED EIGHT STANDARDS THERE, THE EIGHT THINGS THAT WE COULD EVALUATE TO SEE WHETHER, IN FACT, THEY MEET THE ENABLEMENT STANDARD.

Q. AND DID YOU CONSIDER ALL EIGHT OF THOSE FACTORS?

A. YES, I DID.

Q. ALL RIGHT. I'M GOING TO GO THROUGH THEM NOW. THAT'S WHAT THE LAW REQUIRES WE DO. I DON'T MEAN TO BORE YOU, BUT THAT'S WHAT WE'VE GOT TO DO.

I'M GOING TO GO THROUGH THEM A LITTLE BIT OUT OF ORDER AND SAVE A FEW FOR THE END.

BUT LET'S START, THOUGH, WHERE WE SHOULD, WITH NUMBER 1, THE QUANTITY OF EXPERIMENTATION.

DR. STELLA, HOW MUCH EXPERIMENTATION, IN YOUR OPINION, WOULD A PERSON OF SKILL IN THE ART NEED TO PRACTICE THESE CLAIMS IN RELATION TO THE PRODRUG ASPECT OF THEM?

A. WELL, AS I TALKED ABOUT IN MY 400 METER HURDLE RACE, IT WOULD BE INCREDIBLE. I MEAN, I DON'T EVEN KNOW. WE CAN'T EVEN GET INTO THE BLOCKS, INTO THE STARTING BLOCK.

SO TO BEGIN WITH, THAT BY ITSELF WOULD TAKE AN INCREDIBLE AMOUNT OF EXPERIMENTATION TO EVEN KNOW WHERE TO START.

NOW, ASSUMING THAT YOU DO FIND THE STARTING SPOT, THE OPTIONS, THEN, ON A STARTING BLOCK, OR A GROUP OF STARTING BLOCKS, YOU NEED EIGHT PEOPLE IN THE RACE, RIGHT, BUT THE AMOUNT OF EXPERIMENTATION WOULD THEN WILL BE TO REQUIRE YOU TO IDENTIFY A PRODRUG THAT ACHIEVES THE GOALS THAT YOU WANT TO ACHIEVE IS INCREDIBLY HIGH, I MEAN, AN INCREDIBLE AMOUNT OF WORK WITHOUT THAT STARTING BLOCK.

Q. NOW, TO BE FAIR, THERE WERE TYPES OF PRODRUGS KNOWN IN THE PRIOR ART; CORRECT?

A. THERE WAS.

Q. AND AREN'T THERE TESTS THAT A PERSON OF SKILL CAN RUN TO TRY TO FIGURE OUT WHICH PRODRUG THEY MIGHT TRY TO USE?

A. THERE ARE TESTS. THAT'S NOT UNUSUAL. BUT THE TYPE OF TEST, WHAT YOU'RE TRYING TO ACHIEVE, WHERE YOU'RE GOING WOULD REQUIRE YOU TO HAVE, ONE, THE STARTING BLOCK, AND THEN COME UP WITH THE PRODRUGS; AND THEN ESSENTIALLY TRY TO DEFINE HOW YOU GAIN SUCCESS IN THAT.

SO DEFINE THE APPROPRIATE TESTS AND PERFORMING THOSE APPROPRIATE TESTS IS JUST MIND BOGGLING AS TO WHAT WOULD BE REQUIRED.

Q. AND IS THAT UNDUE EXPERIMENTATION?

A. I THINK THAT EXCEEDS THE DEFINITION OF UNDUE EXPERIMENTATION.

Q. OKAY. LET'S GO TO FACTOR 2, THE AMOUNT OF DIRECTION OR GUIDANCE NEEDED.

HOW MUCH AMOUNT OF DIRECTION WOULD THIS HYPOTHETICAL PERSON OR TEAM NEED TO COME UP WITH A PRODRUG APPROACH FOR THE CLAIMS?

A. WELL, THERE IS SOME GUIDANCE. I MEAN, THERE'S HISTORY OF PRODRUGS, RIGHT? SO THERE IS SOME GUIDANCE OUT THERE.

BUT THERE'S NOTHING FROM WHAT I COULD TELL FROM 2000, IN THE TIME PERIOD OF THIS PATENT, THAT WOULD GIVE WHAT I WOULD CALL ADEQUATE DIRECTION AND GUIDANCE, AND THE PATENT SURE AS HECK DOESN'T PROVIDE ANY BECAUSE THERE'S NOTHING IN THERE TO

PROVIDE ANY GUIDANCE.

Q. DOES THAT MEAN A LOT OF GUIDANCE WOULD BE NEEDED OR ONLY A LITTLE?

A. A HUGE AMOUNT OF GUIDANCE. WELL, NOT HUGE. YOU NEED ENOUGH TO BE COMFORTABLE THAT YOU KNOW WHERE YOU'RE GOING WITH THIS.

Q. ALL RIGHT. LET'S SKIP FACTOR 3 AND COME BACK TO THAT. ALL RIGHT? IS THAT OKAY?

A. YES.

Q. AND LET'S GO TO FACTOR 4. THE NATURE OF THE INVENTION HERE IS A METHOD OF TREATMENT FOR HEPATITIS C WITH NUCLEOSIDE AND NUCLEOTIDE COMPOUNDS, INCLUDING PRODRUGS. WE SAW THAT IN THE CLAIM.

HOW DOES THE NATURE OF THIS CLAIMED INVENTION IMPACT THE ANALYSIS?

A. WELL, I THINK IT HAS A VERY BIG EFFECT.

Q. WHY IS THAT?

A. NUMBER ONE, YOU'RE TREATING HEPATITIS C. THERE WERE VERY FEW THINGS OUT THERE. THERE WERE A COUPLE OF DRUGS THAT HAD SOME EFFECT. THEY ALL HAD THEIR OWN TOXICITY AND THEIR OWN LIMITATIONS.

BUT JUST TREATMENT OF HEPATITIS C IN GENERAL, IT SEEMS TO ME THAT AT THE TIME OF THIS PATENT THERE WAS EFFECTIVELY -- THAT IN ITSELF WAS A HIGH HURDLE. WE DIDN'T HAVE ESSENTIALLY EFFECTIVE TREATMENT TO BEGIN WITH.

COMBINING THAT WITH ALL OF THE OTHER COMPLEXITY MAKES THE DESIGN OF A PRODRUG TO BE EFFECTIVE VERY, VERY CHALLENGING.

Q. OKAY. AND LET'S SKIP NUMBER 5 AND COME BACK TO THAT.

NUMBER 6, RELATIVE SKILL OF THOSE IN THE ART. WE ALREADY TALKED ABOUT THAT?

A. RIGHT, RIGHT.

Q. THAT WAS THE HYPOTHETICAL TEAM WE TALKED ABOUT?

A. RIGHT.

Q. AND THAT'S A HIGH LEVEL OF SKILL.

HOW DOES THAT IMPACT YOUR ANALYSIS?

A. WELL, TO QUOTE THE AFRICAN PROVERB, IT TAKES A VILLAGE TO RAISE A CHILD. IT TAKES AN EXTREMELY GOOD TEAM TO DEVELOP A DRUG.

SO THAT PERSON OF SKILL IN THE ART WOULD REQUIRE -- BE REQUIRED, IF YOU WOULD LIKE, TO REALLY PUT TOGETHER A VERY EFFECTIVE TEAM TO ATTACK A PROBLEM LIKE THIS, AND I THINK THAT WOULD REQUIRE A HIGH DEGREE OF SKILL SET THAT I THINK IS NOT MET IN THIS CASE.

Q. ALL RIGHT. AND LET'S SKIP NUMBER 7 AND GO TO 8.

HOW DOES THE BREADTH OF THE CLAIMS AFFECT YOUR ANALYSIS, DR. STELLA?

A. OH, THE CLAIM. HUGE, RIGHT? AND SO FROM THE PRODRUG'S RESPECT, YOU HAVE THE CLAIMS OF THE ACTIVE MATERIAL, AND ON TOP OF THAT, IF ALL PRODRUGS ARE INCLUDED, SO A MILLION TIMES A MILLION, IT DOESN'T TAKE A LOT OF HIGH LEVEL MATH TO REALIZE

THAT THE BREADTH OF THE CLAIMS MAKE THIS AN EXTREMELY --
THERE'S NO GUIDANCE HERE AT ALL --
Q. OKAY.
A. -- IN THE PATENT.
Q. OKAY. LET'S JUMP BACK TO FACTOR 3 AND THEN WE'LL GO TO SOME THINGS THAT WE CAN SHOW THE JURORS.

PRESENCE OR ABSENCE OF WORKING EXAMPLE. FIRST, JUST ONE QUESTION. DOES THE PATENT SHOW ANY WORKING EXAMPLES OF PRODRUGS THAT FALL WITHIN THE SCOPE OF THE CLAIMS?
A. ABSOLUTELY NOT.
Q. NOW, TO BE FAIR, THERE ARE EXAMPLES OF PRODRUGS IN THE PATENTS. SOME OF THE EXAMPLES DEPICT PRODRUGS?
A. YES.
Q. DO ANY OF THOSE FALL WITHIN THE CLAIMS?
A. THEY DO NOT.
Q. LET'S SHOW THE LADIES AND GENTLEMEN OF THE JURY THAT. IF WE GO TO THE NEXT SLIDE.

YOU'VE LISTED HERE, AND WE'LL HIGHLIGHT AS WE GO THROUGH THEM, THE DIFFERENT TYPES OF PRODRUGS THAT ARE EXEMPLIFIED IN THE PATENT.

AND THE FIRST ONE YOU'VE CALLED ACYL DERIVATIVE PRODRUGS, EXAMPLES 59, 60, 120. ARE ANY OF THOSE EXAMPLES WITHIN THE SCOPE OF THE CLAIMS?
A. NO.
Q. NOW WE HAVE ANOTHER COLUMN THAT SAYS DATA. ALL RIGHT?

NOW, PUT THAT ASIDE. LET'S PUT ASIDE THAT THESE ARE NOT EVEN WITHIN THE SCOPE OF THE CLAIMS. CAN YOU DO THAT FOR ME?

A. YES.

Q. IS THERE ANY DATA IN THE PATENT THAT IS EVEN SPECIFIC TO THESE PRODRUGS THAT AREN'T IN THE SCOPE OF THE CLAIMS?

A. THERE IS NO DATA.

Q. AND WE SAW YESTERDAY, I THINK, A LINE FROM THE PATENT REPRESENTATIVE COMPOUNDS OF THE INVENTION TESTED AT IC50 OR EC50 LESS THAN 100 MICROMOLAR.

A. YES.

Q. AND YOU'VE READ THAT IN THE PATENT; IS THAT CORRECT?

A. YES.

Q. AND DOES THAT TELL A PERSON OF SKILL IN THE ART WHAT THOSE REPRESENTATIVE COMPOUNDS EVEN ARE?

A. NO.

Q. OKAY. ANY WAY TO FIGURE OUT FROM THE PATENT WHAT COMPOUNDS THAT LINE IS TALKING ABOUT IN YOUR EXPERT OPINION?

A. I -- I COULDN'T FIGURE IT OUT.

Q. OKAY.

A. AND I'M AN EXPERT.

Q. ALL RIGHT.

A. A PERSON OF SKILL IN THE ART IS NOT GOING TO BE ABLE TO DO IT.

Q. NEXT GROUP OF DRUGS ARE THE SATE PRODRUGS, EXAMPLES 72 TO 81. ANY OF THOSE FALLS WITHIN THE SCOPE OF THE ACTUAL CLAIMS

THAT WE'RE TALKING ABOUT IN THIS CASE?

A. NOT AT ALL.

Q. ANY DATA SPECIFIC TO THOSE THAT YOU COULD FIND?

A. NO, NOT AT ALL.

Q. BY THE WAY, ARE SATE PRODRUGS KNOWN TO HAVE PROBLEMS WITH TOXICITY, DR. STELLA?

A. YES. I'VE WRITTEN ON THAT A LITTLE BIT, AND THE SATE PRODRUGS, SATE IS A TYPE OF TECHNOLOGY TO DERIVATIZE OR TO MAKE PRODRUGS.

THE -- IN THE PROCESS OF RELEASING THE DRUG THAT IS BREAKING DOWN TO RELEASE THE ACTIVE INGREDIENT, IT PRODUCES A MATERIAL CALLED EPISULFIDE, E-P-I-S-U-L-F-I-D-E, AND THERE'S ALWAYS BEEN CONCERNS ABOUT THAT MATERIAL BEING TERATOGENIC AND CARCINOGENIC, AND THAT'S EQUIVALENT TO -- YOU MAY HAVE HEARD ABOUT STERILIZATION BY ETHYLENE OXIDE, AND IT'S VERY ANALOGOUS TO THAT AND I FEEL, AND THE DATA HAS BORNE THIS OUT, THAT THESE TYPE OF PRODRUGS ARE LIKELY TO BE TOXIC AND WILL NEVER MAKE IT TO THE MARKETPLACE.

Q. ALL RIGHT. THE NEXT TYPE OF PRODRUG IS CALLED POC PRODRUGS, OR P-O-C, EXAMPLE 83. IS EXAMPLE 83 WITHIN THE SCOPE OF THE CLAIMS?

A. NO.

Q. IS THERE ANY DATA SPECIFIC TO THE PRODRUG DEPICTED, EVEN THOUGH IT'S NOT IN THE CLAIMS, SPECIFIC TO EXAMPLE 83?

A. NO.

Q. AND THEN THE LAST TYPE OF PRODRUG THAT IS EXEMPLIFIED, LONG CHAIN MONOPHOSPHATE ESTER PRODRUGS, EXAMPLES 84 AND 85.

ARE ANY OF THOSE DEPICTED -- ARE EITHER OF THOSE EXAMPLES DEPICTED, DO THEY ACTUALLY FALL WITHIN THE SCOPE OF THE CLAIMS THAT WE'RE TALKING ABOUT IN THIS CASE?

A. NO, THEY DO NOT.

Q. AND IS THERE ANY DATA SPECIFIC TO THEM?

A. NO.

Q. ALL RIGHT. NOW, DR. STELLA, THE BOTTOM LINE -- YOU KNOW WHAT? LET'S GO. LET ME ASK YOU A DIFFERENT QUESTION.

ARE THERE EVEN OTHER POTENTIAL PRODRUGS NOT DISCUSSED IN THE SPECIFICATION?

A. OH, ABSOLUTELY, YEAH.

Q. NOW, WE'VE HEARD DR. SOFIA TALK ABOUT SOFOSBUVIR BEING A PHOSPHORAMIDATE.

YOU DON'T NEED TO APOLOGIZE.

A. SORRY. THAT'S A TOUGH ONE.

Q. DO YOU AGREE WITH THAT CHARACTERIZATION OF SOFOSBUVIR AS A PHOSPHORAMIDATE PRODRUG?

A. THAT'S A TERM THAT'S BEEN ATTRIBUTED TO THAT, YES.

Q. AND DOES THE SPECIFICATION SHOW ANY EXAMPLES OF PHOSPHORAMIDATE PRODRUGS?

A. IT DOESN'T.

Q. AND, BOTTOM LINE, ARE ANY EXAMPLES COVERED BY THE CLAIMS?

A. NO.

Q. ANY DATA ABOUT THEM?

A. NO.

Q. LET'S TALK MORE ABOUT FACTORS 5 AND 7, AND WE JUST DID THE ABSENCE OF WORKING EXAMPLES.

FACTORS 5 AND 7, JUST TO REMIND EVERYONE, ARE THE STATE OF THE ART AND THE UNPREDICTABILITY OF THE ART.

DR. STELLA, DOES THE SPECIFICATION TALK ABOUT AN ARTICLE ABOUT PRODRUGS?

A. YES, IT DOES.

Q. AND IS THIS A PAPER WRITTEN BY WAGNER?

A. YES.

Q. AND ARE YOU FAMILIAR WITH THAT PAPER?

A. YES, I AM FAMILIAR.

Q. AND DID YOU USE IT IN FORMING YOUR OPINIONS?

A. YES, I DID.

Q. AND I THINK IT'S IN YOUR BINDER AS EXHIBIT 24.

I DON'T BELIEVE THERE'S ANY OBJECTION TO THIS.

PLAINTIFFS MOVE EXHIBIT 24 INTO EVIDENCE.

MR. RABINOWITZ: NO OBJECTION.

THE COURT: IT WILL BE ADMITTED.

(PLAINTIFF'S EXHIBIT 24 WAS RECEIVED IN EVIDENCE.)

BY MR. SINGER:

Q. BEFORE WE LOOK AT WAGNER, LET'S LOOK AT WHAT THE PATENT SAYS ABOUT WAGNER. I THINK THAT WOULD BE HELPFUL TO EVERYONE.

IF WE GO TO THE NEXT SLIDE, WE'VE DEPICTED HERE VERBATIM

EXAMPLE 72. THIS IS ONE OF THESE SATE PRODRUGS THAT YOU TALKED ABOUT, THE TOXIC ONE, GENERAL PROCESS TO SATE PRODRUG MOIETY.

I'M JUST GOING TO SAY SATE. SATE PRONUCLEOTIDES ARE DISCUSSED IN C.R. WAGNER, ET AL, PRONUCLEOTIDES TOWARD THE IN VIVO DELIVERY OF ANTI-VIRAL AND ANTI-CANCER NUCLEOTIDES.

DO YOU SEE THAT?

A. YES.

Q. AND THEN IT SAYS, WHICH IS INCORPORATED BY REFERENCE HEREIN IN ITS ENTIRETY.

FIRST OFF, HOW WOULD A PERSON OF SKILL IN THE ART ACTUALLY READ WHAT IS BEING TALKED ABOUT HERE AS TO WAGNER? HOW DO YOU BELIEVE A PERSON OF SKILL WOULD READ THIS?

A. WELL, I BELIEVE, BASED ON THE TITLE, GENERAL PROCESS TO SATE PRODRUG MOIETY, AND THEN THE SUBSEQUENT REFERENCE TO WAGNER, TO ME, WAGNER BY BEING, QUOTE-UNQUOTE, "INCORPORATED BY REFERENCE," REFERS TO, IN FACT, WAGNER AS IT RELATES TO SATE PRODRUGS.

Q. OKAY. SO IN YOUR OPINION, WE SHOULD ONLY BE LOOKING AT THE WAGNER PAPER AS IT RELATES TO SATE?

A. THAT'S CORRECT.

Q. AND YOU ALREADY TALKED ABOUT SATE PRODRUGS EARLIER; CORRECT?

A. THAT'S CORRECT.

Q. AND I KNOW THERE'S A DISAGREEMENT ABOUT THIS BETWEEN THE TWO SIDES.

A. RIGHT.
Q. LET'S PUT ASIDE -- LET'S PUT ASIDE THAT IT TALKS ABOUT WAGNER UNDER A HEADER TALKING ABOUT SATE IN AN EXAMPLE.
A. YES.
Q. AND CAN WE PUT THAT ASIDE? CAN YOU DO THAT?
A. YES.
Q. AND CAN WE CONSIDER IT IN ITS ENTIRETY? AND DID YOU?
A. I DID.
Q. ALL RIGHT. DOES WAGNER, JUST THIS PUBLICATION THAT'S REFERRED TO IN ONE LINE IN THIS PATENT, ENABLE A PERSON OF SKILL IN THE ART TO PRACTICE THE CLAIMED INVENTION AS FAR AS THE USE OF ALL OF THESE PRODRUGS?
A. ABSOLUTELY NOT.
Q. AND LET'S TAKE A LOOK AT THE ARTICLE. ALL RIGHT?

IF WE GO TO THE NEXT SLIDE, WE SEE THE TITLE JUST AS IT WAS IN THE PATENT, "PRONUCLEOTIDES: TOWARD THE IN VIVO DELIVERY OF ANTI-VIRAL AND ANTI-CANCER NUCLEOTIDES?"

FIRST OFF, I KNOW YOU TOLD US TO PUT THE TITLE ON THERE. WHY DID YOU TELL US TO PUT THE TITLE ON THERE IN YOUR PRESENTATION?
A. WELL, FIRST OF ALL, THE COMPOUNDS THAT ARE BROADLY CLAIMED COVER NUCLEOSIDES AND NUCLEOTIDES, S-I-D-E-S VERSUS T-I-D-E-S, OKAY?

AND JUST TO REFRESH, IF YOU DON'T REMEMBER THAT, YOU REMEMBER THAT THE NUCLEOSIDE IS ONE OF THESE SORT OF BASE

MOLECULES WHICH DOESN'T HAVE IN THE Y POSITION, LEFT-HAND SIDE IN ALL OF THE DIAGRAMS, THAT Y IS NOT A PHOSPHATE. IT'S WHAT IS CALLED OH OR HYDROXYL GROUP, OKAY.

THE NUCLEOTIDE IS WHERE THAT Y IS AN O PHOSPHATE. THAT'S THE NUCLEOTIDE, OKAY?

WAGNER, IN HIS ANALYSIS OF THE STATE OF THE ART OF DELIVERING -- THE STATE OF THE ART OF DELIVERING POTENTIALLY EXAMPLES OR PROCESSES, EXAMPLES OF NUCLEOTIDES AND NOT NUCLEOSIDES.

SO WAGNER BY ITSELF DOESN'T ADDRESS NUCLEOSIDE PRODRUGS AT ALL. SO IF YOU LIKE, A SMALL SUBSET OF A MUCH BIGGER SUBSET.

SO WAGNER ONLY TALKS ABOUT ONE LITTLE GROUP IN ONE CORNER OF A VERY BIG SET OF MOLECULES. SO WAGNER ONLY FOCUSES ON NUCLEOTIDES.

Q. ALL RIGHT. LET'S GO TO THE NEXT SLIDE, WHICH IS THE ABSTRACT. I'M SURE MANY MEMBERS OF THE JURY KNOW WHAT AN ABSTRACT IS, BUT SOME WAY NOT. WHAT IS AN ABSTRACT IN A SCIENTIFIC PAPER?

A. WELL, IT'S REALLY SORT OF THE SUMMARY, IF YOU LIKE, OF WHAT THE AUTHORS FOUND.

SO, FOR EXAMPLE, WHEN YOU GO INTO A BOOK STORE -- AND WE STILL HAVE BOOK STORES, RIGHT? -- AND IF YOU GO INTO THE BOOK STORE AND YOU PULL IT UP ON THE KINDLE AND YOU'RE LOOKING FOR A BOOK BY GIANNI DE LEON BENEDETTI, "DETECTIVE IN VENICE" AND YOU WANT TO READ THAT BOOK, WHAT COMES UP?

YOU GET AN ABSTRACT AND A SMALL SUMMARY THAT SAYS, HEY, THAT'S COOL, AND THAT MAY BE A PAPER OR A BOOK I'D LIKE TO READ.

OR YOU PICK UP THE BOOK AT THE BOOKSTORE AND YOU LOOK AT THE BACK COVER AND THE BACK COVER HAS AN IDEA OF WHAT THE BOOK IS ABOUT. IT DOESN'T GIVE YOU THE SECRETS, BUT IT GIVES YOU AN IDEA OF WHAT THE BOOK IS ABOUT AND IT TELLS YOU ABOUT THE AUTHOR.

SO THE ABSTRACT HAS THE SAME ELEMENT.

AND THIS IS SAYING, OKAY, ALL OF THIS ANALYSIS OF PRODRUGS AND NUCLEOTIDES, THIS IS WHAT WE FOUND, AND SO IF YOU LIKE IT, IT HELPS YOU UNDERSTAND, IS THIS A PAPER I REALLY WANT TO READ OR IS THIS SOMETHING, NO, THIS DOESN'T INTEREST ME?

SO AN ABSTRACT HELPS YOU KNOW WHAT THEY CONCLUDED WITHOUT HAVING TO READ THE WHOLE PAPER.

Q. ALL RIGHT. DR. STELLA, WHAT HAVE YOU CHOSEN TO HIGHLIGHT FOR THE JURY IN THE ABSTRACT OF WAGNER?

A. WELL, CAN I READ OUT THE --

Q. ABSOLUTELY.

A. THE FIRST SECTION?

"TO OVERCOME THE MANY HURDLES PREVENTING THE USE OF ANTI-VIRAL AND ANTI-CANCER NUCLEOSIDES AS THERAPEUTICS, THE DEVELOPMENT OF A PRODRUG METHODOLOGY (I.E., NUCLEOTIDE) FOR THE IN VIVO DELIVERY OF NUCLEOTIDES HAS BEEN PROPOSED AS A SOLUTION."

Q. STOP RIGHT THERE. IT'S TALKING ABOUT THESE HURDLES. THAT'S THE SAME CONCEPT THAT YOU USED; RIGHT?

A. RIGHT.

Q. AND THEN THE ABSTRACT GOES ON TO TALK ABOUT THE IDEAL NUCLEOSIDE -- OR NUCLEOTIDE, MY BAD -- AND THEN YOU'VE HIGHLIGHTED ANOTHER LINE. AND WHAT DOES THAT SAY?

A. "ALTHOUGH THIS GOAL HAS YET TO BE ACHIEVED."

Q. OKAY. WHAT DOES THAT SAY? EVEN THOUGH IT SAYS MANY CLEVER AND IMAGINATIVE APPROACHES HAVE BEEN DEVELOPED, WHAT DOES THAT TELL A PERSON OF SKILL IN THE ART ABOUT WHERE THINGS STOOD, WHERE THINGS STOOD AT THE TIME OF THIS ARTICLE IN 2000 JUST SHORTLY BEFORE THE PATENTS AT ISSUE IN THIS CASE WERE APPLIED FOR?

A. WELL, TO ME WHAT WAGNER WAS SAYING IS, HEY, WE'VE TRIED A LOT OF THINGS AND THERE ARE SOME THINGS LOOK LIKE -- SOME EXAMPLES SHOW SOME PROMISE, BUT THERE'S REALLY -- WE'RE NOT THERE YET.

Q. NOW, IN THE BODY OF WAGNER, DOES IT LIST EVEN MORE POSSIBLE APPROACHES A PERSON OF SKILL IN THE ART MIGHT TRY?

A. YES, IT DOES.

Q. ALL RIGHT. IF WE GO TO THE NEXT SLIDE. THIS IS A DEMONSTRATIVE THAT YOU HELPED PREPARE OF WHAT YOU CALLED A LAUNDRY LIST OF POSSIBLE PRODRUG GROUPS THAT MIGHT BE TRIED.

WHY DID YOU CALL IT A LAUNDRY LIST?

A. WELL, WAGNER'S PAPER IS A REVIEW. IT'S BASICALLY AN

ANALYSIS THAT SOMEONE THAT HAS CONSIDERED A GROUP, THAT IS OFTEN HIGHLY SKILLED IN THE ART, HAS DONE A LITERATURE SURVEY AND THEY HAVE GONE OUT AND BASICALLY DONE A SURVEY AND SAID, WHAT ARE THE SORT OF APPROACHES THAT PEOPLE HAVE TRIED? WHAT ARE THE THINGS THAT PERHAPS HAVE BEEN TRIED TO DATE, UNDERSTANDING THAT ANY REVIEW ARTICLE, THE DAY YOU PUBLISH IT, IT'S PROBABLY OUT OF DATE, RIGHT? BECAUSE SOMEBODY ELSE HAS PROBABLY COME UP WITH SOME OTHER WORK.

SO THIS IS A LAUNDRY LIST OF COMPOUNDS OR APPROACHES, IF YOU LIKE, OR HEADINGS WHERE PEOPLE HAVE LOOKED AT VARIOUS APPROACHES FOR THE DELIVERING OF NUCLEOTIDES.

Q. OKAY. NOW, IN LISTING -- WE'RE NOT GOING TO READ THESE. I PROMISED THE REPORTER I WOULDN'T DO THAT.

IN LISTING ALL OF THESE POSSIBILITIES THAT WE SEE HERE IN PDX-616, IS THERE A SINGLE EXAMPLE IN THIS ARTICLE IN WAGNER OF A PRODRUG OF A 2' METHYL, 2' FLUORO NUCLEOTIDE OR NUCLEOSIDE?

A. ABSOLUTELY NOT.

Q. ALL RIGHT. DOES THIS ARTICLE EVEN TELL, EVEN TELL A PERSON OF SKILL IN THE ART HOW TO SELECT ONE OF THESE MANY APPROACHES FOR ANY PARTICULAR NUCLEOTIDE OR NUCLEOSIDE?

A. NO, IT DOESN'T.

AND LET ME JUST REITERATE. WHAT I HAVE DONE HERE WITH THESE FIVE HEADINGS IS SORT OF CATEGORIES. WITHIN EACH ONE OF THOSE CATEGORIES YOU SEE ME LISTING A WHOLE BUNCH OF THINGS WITHIN THOSE CATEGORIES.

AND WITHIN THOSE SUBCATEGORIES THERE ARE MULTIPLE POSSIBLE DERIVATIVES, OKAY. SO WHEN I CAME UP EARLIER AND I SAID THERE WAS AN UNLIMITED NUMBER, JUST ON A NUCLEOTIDE SIDE -- FORGET ABOUT THE NUCLEOSIDE SIDE -- ON THE NUCLEOTIDE SIDE, YOU CAN COUNT LITERALLY MILLIONS OF COMPOUNDS.

Q. AND DOES THE ARTICLE THEN HAVE A CONCLUSION WHERE THE AUTHORS MAKE A CONCLUSION AFTER SURVEYING THE LITERATURE?

A. THEY DO, YES.

Q. AND IF WE GO TO THE NEXT SLIDE, PDX-627, SUMMARY AND CHALLENGES. AND YOU'VE HIGHLIGHTED HALF OF THE SENTENCE IN THE SECOND PARAGRAPH THERE, AND THE FIRST PARAGRAPH TALKS ABOUT THE IMAGINATIVE AND CLEVER APPROACHES AS WE SAW IN THE ABSTRACT.

IT SAYS, "DESPITE THE SUCCESS OF PRONUCLEOTIDES, MANY QUESTIONS AND ISSUES REMAIN TO BE ADDRESSED. NO SINGLE METHOD HAS PROVED TO BE GENERALLY USEFUL FOR ALL NUCLEOTIDES."

WHAT DOES THAT TELL A PERSON OF SKILL IN THE ART?

A. SOMEONE READING THIS WOULD SAY, GOOD LUCK. THERE'S A LOT OF THINGS THAT YOU COULD TRY IN THIS NOT BEING OUT THERE THAT STAND AND SAYS THIS IS WHERE WE NEED TO GO.

Q. AND IF WE GO TO THE NEXT SLIDE, DO THEY SAY EVEN MORE IN THE NEXT PARAGRAPH?

A. YES. I'D JUST LIKE TO READ THE AREA I HIGHLIGHTED. "UNFORTUNATELY, THE EFFECTS OF PRONUCLEOTIDE DESIGN ON THE MECHANISM OF NUCLEOTIDE RELEASE HAVE ONLY BEEN SYSTEMATICALLY STUDIED IN A FEW CASES. FURTHERMORE, IN VIVO --" IN VIVO MEANS

IN LIVE ANIMALS -- "IN VIVO POTENCY, LONG-TERM TOXICITY, BIOAVAILABILITY" -- BIOAVAILABILITY IS THE ABILITY TO ABSORB A DRUG -- "PLASMA PHARMACOKINETICS" -- THAT IS THE TIME PROFILE OF A DRUG IN THE BODY, PROFILE OF DRUGS IN THE BODY TO LEAD TO EFFECTIVE THERAPY -- "AND TISSUE DISTRIBUTION HAVE BEEN DETERMINED ONLY IN A FEW PRONUCLEOTIDES."

Q. DR. STELLA, DOES THIS MEAN THAT A PERSON OF SKILL IN THE ART, READING WAGNER, THEY WOULD CONCLUDE THAT THE ART IS PREDICTABLE OR UNPREDICTABLE?

A. WELL, AS I SAID, GOOD LUCK. IT'S HIGHLY UNPREDICTABLE.

Q. ALL RIGHT. DR. STELLA, HAVE WE NOW WALKED THROUGH ALL OF THE FACTORS THAT YOU HAVE STUDIED?

A. WE DID.

Q. AND CAN WE SUMMARIZE YOUR OPINION ON THE NEXT SLIDE?

A. YES.

Q. AND THERE'S THE STANDARD AGAIN. OKAY. AND THOSE ARE THE EIGHT FACTORS. AND IF WE CAN GO TO PDX 620. AND IF YOU CAN EXPLAIN TO THE JURY IN SUMMARY FORM WHY YOU BELIEVE THE PATENT IS NOT ENABLED?

A. WELL, IT'S NOT ENABLED BECAUSE IT'S GOING TO TAKE A HIGH AMOUNT OF EXPERIMENTAL -- EXPERIMENTATION TO IDENTIFY A WORKING COMPOUND; THERE'S SUBSTANTIAL GUIDANCE THAT IS NEEDED AND VERY LITTLE IS GIVEN; THERE ARE NO WORKING EXAMPLES AND NO DATA; THE FIELD ITSELF IS COMPLEX AND UNPREDICTABLE; THERE'S A LIMITED GUIDANCE IN THE PRIOR ART; AND THE VERY BROAD CLAIMS COVERING

THE USE OF ANY POSSIBLE PRODRUGS TO TREAT IS VERY, VERY BROAD.

SO IN MY EYES THIS PATENT TOTALLY LACKS ENABLEMENT.

Q. DR. STELLA, ARE THE INVENTORS BASICALLY SAYING TO PERSONS OF SKILL IN THE ART WHO READ THIS, YOU GO FIGURE IT OUT?

A. ABSOLUTELY.

Q. ALL RIGHT. LET'S TALK BRIEFLY ABOUT YOUR OPINION ON WRITTEN DESCRIPTION. YOU ALSO REACHED AN OPINION ON WHETHER OR NOT CLAIMS, YOU KNOW, 1 AND 2 ARE VALID UNDER THE WRITTEN DESCRIPTION; IS THAT CORRECT?

A. YES.

Q. AND, YOU KNOW, DR. STELLA, WE NEVER TALKED ABOUT CLAIM 2, ACTUALLY. WE SKIPPED THAT, AND THAT'S MY FAULT.

IF WE COULD GO BRIEFLY, MR. ANG, IF WE COULD GO TO PDX 604, PLEASE. 603. 603.

WE TALKED ABOUT CLAIM 1 IN THE MARKUSH STRUCTURE, AND WE ACTUALLY DIDN'T TALK ABOUT CLAIM 2.

A. RIGHT.

Q. AND IS YOUR OPINION THE SAME FOR CLAIMS 1 AND 2?

A. ABSOLUTELY.

Q. AND WHAT IS THE DIFFERENCE BETWEEN CLAIMS 1 AND 2?

A. CLAIM 1, I THINK, WE TALKED ABOUT ADEQUATELY.

CLAIM 2, AND I'D LIKE TO READ THIS OUT BECAUSE THERE'S A LEGAL ASPECT OF THIS, THE METHOD OF CLAIM 1 WHEREIN.

AND WHAT THAT MEANS IS THAT CLAIM 1 IS ACTUALLY BUILT INTO CLAIM 2. SO CLAIM 2 IS WHAT IS CALLED, I BELIEVE, A DEPENDENT

CLAIM, THAT IT DEPENDS ON CLAIM 1.

AND EFFECTIVELY WHAT THIS CLAIM IS SAYING IS THAT YOU CAN TAKE THE COMPOUNDS OF CLAIM 1 AND TREAT HCV BY GIVING A SECOND DRUG WITH THAT.

SO THIS CLAIM, I ASSUME, WAS DESIGNED TO COVER THE FACT THAT A COMPOUND FROM CLAIM 1 WOULD THEN BE GIVEN TO TREAT HCV IN COMBINATION WITH A SECOND DRUG.

Q. BY BEING A DEPENDENT CLAIM, DOES THAT MEAN THAT ALL OF CLAIM 1 IS INCORPORATED INTO CLAIM 2?

A. THAT'S CORRECT.

Q. AND IS YOUR OPINION -- THE BASIS FOR YOUR OPINION ON ENABLEMENT THE SAME FOR CLAIM 2 AS IT IS FOR CLAIM 1?

A. YES.

Q. AND LET'S GO AND TALK ABOUT WRITTEN DESCRIPTION BRIEFLY.

IF WE COULD, MR. ANG, GO TO PDX 621.

ALL RIGHT. THIS IS THE WRITTEN DESCRIPTION STANDARD THAT YOU -- THAT IS IN SUMMARY. THE JURY WILL GET MUCH LONGER INSTRUCTIONS.

THAT THE PATENT'S DISCLOSURE MUST CONVEY TO A PERSON OF SKILL IN THE ART THAT THE INVENTORS HAD POSSESSION OF THE CLAIMED SUBJECT MATTER?

IS THAT THE STANDARD YOU APPLIED?

A. YES.

Q. AND WHAT IS YOUR OPINION AS TO WHETHER OR NOT THE PATENT SHOWS THAT THE INVENTORS POSSESSED THE SCOPE OF THEIR CLAIMS AS

IT RELATES TO THE PRODRUG ASPECT OF THINGS?

A. I'VE GOT THAT SUMMARIZED.

Q. IF WE CAN GO TO THE NEXT SLIDE.

A. SO THE CLAIMS COVER TREATING HCV WITH AN EXTREMELY LARGE GENUS OF COMPOUNDS AND ANY PRODRUG OF THOSE COMPOUNDS.

SO TO BEGIN WITH AND TO QUOTE THE DEFINITION THAT THE INVENTORS HAD POSSESSION OF THE CLAIMED COMPOUNDS, THAT COVERS A VERY BROAD RANGE OF COMPOUNDS, AND THERE ARE NO EXAMPLES OF PRODRUGS THAT FALL WITHIN THE SCOPE OF THE CLAIMS, AND THERE'S NO DATA OR ANY PRODRUG, PERIOD, LET ALONE THOSE THAT FALL WITHIN THE CLAIMS SINCE THERE ARE NONE. AND SO IN MY ESTIMATION, THE NAMED INVENTORS HERE WERE NOT IN POSSESSION OF THE INVENTION.

Q. OKAY.

A. AND, THEREFORE, THEY DID NOT MEET THE WRITTEN DESCRIPTION CRITERIA.

Q. SO THIS WAS SOMETHING THAT THEY DIDN'T INVENT, DID THEY?

A. THAT'S RIGHT.

Q. AND, DR. STELLA, A COUPLE OF FINAL QUESTIONS. IN SIMPLE TERMS, DOES THE '499 PATENT SOLVE THE PROBLEM OF HOW TO TREAT HEPATITIS C WITH A PRODRUG OF A NUCLEOTIDE OR A NUCLEOSIDE?

A. ABSOLUTELY NOT.

Q. WHO SOLVED THAT PROBLEM?

A. I BELIEVE PHARMASSET IN THEIR PRODUCT SOFOSBUVIR DID THAT.

Q. AND WHAT DO YOU THINK OF SOFOSBUVIR AS AN EXPERT WHO HAS

WORKED IN THIS FIELD NOW FOR OVER 40 YEARS?

A. I'M A PRODRUG GUY.

Q. I THINK YOU SAID I'M A PRODRUG GUY.

A. I'M A PRODRUG GUY. SOFOSBUVIR IS ONE COOL DRUG. I MEAN, IT KNOCKED IT OUT OF THE BALLPARK. IT'S SAVING JUST AN INCREDIBLE NUMBER OF LIVES AND THE TECHNOLOGY AND HOW THEY GOT THERE, I THINK, IS ONE OF THE COOLEST STORIES THAT I HAVE EVER SEEN AS A SCIENTIST IN MY 40 YEARS.

Q. THANK YOU.

I HAVE NO FURTHER QUESTIONS AT THIS TIME.

THE WITNESS: IS IT POSSIBLE TO TAKE A SHORT BREAK?

THE COURT: ABSOLUTELY.

THE WITNESS: I'M GETTING REALLY -- I'M THIRSTY. IF I CAN SORT OF DRINK SOME WATER.

THE COURT: LET'S TAKE A 10 MINUTE BREAK. YOU'RE THE ONE DOING ALL OF THE TALKING AND WE'RE JUST LISTENING. ALL RIGHT. WE'LL COME BACK IN 10 MINUTES.

(RECESS FROM 10:05 A.M. UNTIL 10:17 A.M.)

THE COURT: PLEASE BE SEATED. ALL OF OUR JURORS ARE BACK. ALL RIGHT. I BELIEVE WE CONCLUDED THE DIRECT EXAMINATION OF DR. STELLA.

AND, MR. RABINOWITZ, ARE YOU TAKING THE LEAD ON THIS ONE?

MR. RABINOWITZ: YES, YOUR HONOR.

THE COURT: ALL RIGHT. WOULD YOU LIKE TO CROSS-EXAMINE THE WITNESS?

MR. RABINOWITZ: THANK YOU, YOUR HONOR.

YOUR HONOR, MAY I APPROACH?

THE COURT: YES.

CROSS-EXAMINATION

BY MR. RABINOWITZ:

Q. GOOD MORNING, DR. STELLA.

A. GOOD MORNING.

Q. WE'VE MET BEFORE. WE'VE, IN FACT, WORKED ON SEVERAL CASES TOGETHER?

A. YES.

Q. AND JUST SO THE JURY KNOWS WHO I AM, I AM STEPHEN RABINOWITZ, AND I REPRESENT MERCK IN THIS MATTER.

DR. STELLA, YOU ARE AWARE THAT THERE ARE TWO PATENTS AT ISSUE IN THIS LITIGATION?

A. THAT'S WHAT I'M TOLD, YES.

Q. AND ONE IS THE '499 PATENT?

A. YES.

Q. AND THAT'S IDENTIFIED BY THE THREE DIGITS ON THE TOP ON THE RIGHT, THE '499 PATENT?

A. YES.

Q. AND THE OTHER IS THE '712 PATENT?

A. YES.

Q. WE CAN AGREE YOUR TESTIMONY AND OPINIONS THAT YOU GAVE THIS MORNING CONCERN THE '499 PATENT?

A. YES.

Q. NOT THE '712 PATENT?
A. THAT'S CORRECT.
Q. CAN I ASK YOU TO TURN TO THE '499 PATENT THAT IS IN EVIDENCE AS EXHIBIT 1. IT'S THE TOP EXHIBIT IN THE BINDER I'VE JUST GIVEN YOU.
AND CAN I ASK YOU TO TURN TO CLAIM 1, AND THAT'S TOWARDS THE BACK IN COLUMN 137.
CAN YOU GO TO COLUMN 137. AND THAT'S ON YOUR SCREEN. DO YOU SEE THAT?
A. CAN YOU BLOW THAT UP A LITTLE BIT MORE. IT'S A LITTLE BIT FUZZY. OKAY.
Q. AND THAT'S THE WORD THAT YOU FOCUSSED ON IN YOUR TESTIMONY THIS MORNING "ADMINISTERING;" CORRECT?
A. CORRECT. THAT'S ONE OF THE THINGS I CONCENTRATED ON.
Q. AND, NOW, CAN WE GO TO COLUMN 37 OF THE '499 PATENT?
A. COLUMN 37.
Q. COLUMN 37. SORRY. COLUMN 32. I BEG YOUR PARDON. THE PARAGRAPH BEGINNING AT LINE 5 OF COLUMN 32.
A. LINE 5?
Q. AND IT'S ON THE SCREEN IN FRONT OF YOU, AND WE'VE BLOWN UP THE FIRST SENTENCE OF THAT PARAGRAPH.
DO YOU SEE THAT?
A. YES.
Q. AND WE CAN AGREE THAT IT SAYS, "THE TERMS OF 'ADMINISTRATION OF' AND 'ADMINISTERING' A COMPOUND SHOULD BE

UNDERSTOOD TO MEAN PROVIDING A COMPOUND OF THE INVENTION OR A PRODRUG OF A COMPOUND OF THE INVENTION TO THE INDIVIDUAL IN NEED."

THAT'S WHAT THE PATENT SAYS; RIGHT?

A. YES.

Q. CAN WE AGREE THAT THIS COMPOUND ALLOWS IT DIRECTLY TO BE ADMINISTERED AS THE COMPOUND?

A. YES.

Q. AND IT ALSO ALTERNATIVELY ALLOWS FOR THE COMPOUND TO BE DELIVERED BY MEANS OF A PRODRUG?

A. THAT IS A WAY THAT I THINK THAT IT'S CORRECT.

Q. AND LET'S GO TO COLUMN 34 OF THE '499 PATENT THE PARAGRAPH BEGINNING AT LINE 31 AND I'D LIKE YOU TO TAKE A LOOK AT THE SENTENCE BEGINNING "THE COMPOSITIONS INCLUDE."

AND THAT'S ON YOUR SCREEN AS WELL.

A. ARE YOU ASKING ME TO JUST READ THE FIRST SENTENCE?

Q. I'M JUST DIRECTING YOUR ATTENTION. DO YOU HAVE THAT?

A. YES.

Q. AND IT'S ON THE SCREEN AS WELL IF YOU WANT TO LOOK THERE.

A. ALL RIGHT.

Q. AND WE CAN AGREE THAT THIS ALLOWS FOR THE COMPOSITION TO BE ADMINISTERED ORALLY; RIGHT?

A. YES.

Q. AND IT ALLOWS FOR THE COMPOSITION TO BE ADMINISTERED BY A RECTAL ROUTE?

A. THAT'S WHAT IT SAYS. I WOULD NOT RECOMMEND IT, BUT THAT'S OKAY.

Q. IT ALLOWS THE COMPOSITION TO BE ADMINISTERED BY A TOPICAL ROUTE?

A. AGAIN, IT STATES THAT, BUT I WOULDN'T RECOMMEND THAT.

Q. AND TOPICAL MEANS SPREADING IT ON THE SKIN?

A. THAT'S CORRECT.

Q. AND IT ALLOWS FOR PARENTERAL?

A. YES. AND FOR THE JURY, PARENTERAL MEANS AN INJECTABLE FORM.

Q. ALL RIGHT. AND WITH PARENTERAL IT ALLOWS FOR IT TO BE ADMINISTERED SUBCUTANEOUSLY?

A. YES, UNDER THE SKIN.

Q. AND IT ALLOWS FOR IT INTRAMUSCULARLY?

A. YES, THAT'S INJECTION INTO THE MUSCLE AND USUALLY THE GLUTEUS MAXIMUS.

Q. AND IT ALLOWS FOR INTRAVENOUSLY?

A. THAT'S WHAT IT SAYS.

Q. AND INTRAVENOUS MEANS DIRECTLY INTO A VEIN?

A. THAT'S CORRECT.

Q. AND SOMETIMES CALLED AN IV?

A. YES.

Q. AND WE CAN AGREE THIS ALLOWS FOR PULMONARY ADMINISTRATION?

A. I'M SORRY?

Q. THIS ALLOWS FOR PULMONARY ADMINISTRATION?

A. OPHTHALMIC AND PULMONARY.
Q. AND PULMONARY ADMINISTRATION MEANS THROUGH THE LUNGS?
A. YES. AGAIN, I WOULDN'T RECOMMEND THAT.
Q. AND IT ALLOWS FOR ADMINISTRATION BY AN OCULAR ROUTE?
A. YES.
Q. AND THAT MEANS ADMINISTRATION THROUGH THE EYE?
A. TO THE EYE.
Q. AND WE CAN AGREE THAT IT ALLOWS FOR ADMINISTRATION BY A NASAL ROUTE?
A. THAT'S WHAT IT STATES.
Q. AND THAT MEANS BREATHING IT IN THROUGH THE NOSE?
A. YES.
Q. WE CAN AGREE THAT ALL OF THESE ARE WAYS IN WHICH THE PATENT PERMITS THE COMPOSITION TO BE ADMINISTERED ACCORDING TO THIS LANGUAGE?
A. COULD YOU RESTATE THAT, PLEASE. I JUST WANT TO MAKE SURE.
Q. WE CAN AGREE THAT THIS LANGUAGE PERMITS THE COMPOSITION TO BE ADMINISTERED BY ANY OF THESE ROUTES?
A. THE PATENT STATES THAT, YES.
Q. NOW, IN YOUR TESTIMONY YOU IDENTIFIED SEVERAL HURDLES THAT YOU SPOKE ABOUT AND YOU USED A DIAGRAM. COULD I ASK YOU TO TAKE A LOOK AT THAT HURDLE DIAGRAM, PDX 607. AND COULD WE HAVE IT UP ON THE SCREEN, PLEASE. AND YOU SAID THESE ARE HURDLES IN DEVELOPING ORAL PRODRUGS?
A. YES.

Q. CAN WE AGREE THAT THE FIRST HURDLE SYNTHESIS OF THE PRODRUG COMPOUND DOESN'T APPLY TO A DRUG THAT IS GIVEN AS AN ACTIVE COMPOUND AND NOT AS A PRODRUG?

A. WELL, YOU HAVE THE SYNTHESIS OF THE DRUG BUT, YES, WHEN IT RELATES TO PRODRUG BUT THAT ALSO REQUIRES YOU HAVE A STARTING POINT.

Q. AND IF YOU'RE GIVING IT AS THE COMPOUND AND NOT AS THE PRODRUG, YOU DON'T NEED TO SYNTHESIZE THE PRODRUG?

A. THAT'S CORRECT.

Q. AND THEN HURDLE NUMBER 2 IS DISSOLUTION AND CHEMICAL STABILITY IN THE GI TRACT. CAN WE AGREE THAT GI MEANS GASTROINTESTINAL TRACT?

A. YES, I DID DEFINE THAT FOR THE JURY.

Q. AND WE CAN AGREE FOR A DRUG THAT IS NOT GIVEN ORALLY, IT DOESN'T NEED TO DISSOLVE AND BE STABLE IN THE GASTROINTESTINAL TRACT, THAT HURDLE DOESN'T APPLY?

A. NO, FOR THE -- SORRY. COULD YOU REDO THE QUESTION BECAUSE I GET CONFUSED.

Q. LET ME RESTATE IT, AND IT MAY BE EASIER THAT WAY.

CAN WE AGREE THAT IF A DRUG IS GIVEN BY A PARENTERAL OR NOT ORALLY, IT DOES NOT HAVE TO PASS HURDLE 2 DISSOLUTION AND CHEMICAL STABILITY IN THE GI TRACT?

A. IT DOESN'T HAVE TO PASS THAT, BUT IT DOES HAVE TO PASS ANOTHER SET OF HURDLES IN THAT CASE.

Q. AND HURDLE 3 YOU IDENTIFIED WAS STABILITY TO SURVIVE

ENZYME ATTACK IN THE GI TRACT; CORRECT?

A. CORRECT.

Q. AND WE CAN AGREE THAT HURDLE 3 DOESN'T APPLY IF THE PRODRUG IS NOT GIVEN ORALLY?

A. NOT IN A GI TRACT BUT IT ALSO -- WITH ALL OF THE OTHER ROUTES IT WOULD BE A COMPARABLE POTENTIAL SET OF HURDLES THAT WOULD HAVE TO BE TAKEN CARE OF, YES.

Q. AND WE CAN AGREE THAT THIS PARTICULAR HURDLE DOESN'T APPLY TO A PRODRUG THAT IS NOT GIVEN ORALLY?

A. THAT'S CORRECT.

Q. AND HURDLE 4 WAS PERMEABILITY THROUGH MEMBRANES AND ENTEROCYTE CELLS LINING THE GI TRACT; CORRECT?

A. YES.

Q. AND WE CAN AGREE THAT THIS PARTICULAR HURDLE DOESN'T APPLY IF THE DRUG WAS NOT GIVEN ORALLY?

A. NO, BUT THERE WOULD BE A COMPARABLE SET OF HURDLES FOR A DRUG GIVEN BY SOME OTHER ROUTE. FOR EXAMPLE, IN THE NASAL CAVITY YOU WOULD HAVE THE PERMEABILITY THROUGH THE NASAL PASSAGE INTO THE BLOOD SUPPLY OR THROUGH THE CELLS THAT LINE IN THE NASAL PASSAGE.

Q. LET'S LOOK AT NUMBER 5, STABILITY TO SURVIVE THE ENZYMES IN ENTEROCYTE CELLS. WE CAN AGREE THAT ENTEROCYTE CELLS ARE CELLS THAT LINE THE GUT?

A. YES.

Q. AND WE CAN AGREE THAT THIS PARTICULAR HURDLE DOESN'T APPLY

TO A DRUG IF IT'S NOT GIVEN ORALLY?

A. IF IT'S NOT GIVEN ORALLY, YOU'RE RIGHT, BUT THERE WOULD BE ANOTHER SET OF CELLS. FOR EXAMPLE, IN INTRAVENOUS INJECTION, THE FIRST ORGAN YOU SEE IS THE LUNG, AND THE LUNG HAS SOME OF THE SAME PROCESSES.

IF YOU TAKE THE DRUG BY A NASAL ADMINISTRATION, YOU'VE GOT PERMEABILITY, ENZYMES THAT ARE PRESENT IN THOSE CELLS, RIGHT.

Q. AND WE CAN AGREE THAT THERE ARE NO ENTEROCYTES?

A. NOT ON INTRAVENOUS INJECTION, RIGHT.

Q. AND HURDLE NUMBER 6 IS PASSING THROUGH ENTEROCYTES INTO BLOOD THAT FLOWS INTO LIVER. WE CAN AGREE THAT THAT HURDLE CONTAINING ENTEROCYTES DOESN'T APPLY TO A PRODRUG THAT IS NOT GIVEN ORALLY?

A. CORRECT. BUT, AGAIN, IT'S A COMPARABLE HURDLE.

Q. AND THEN HURDLE NUMBER 8 YOU SAID AT THE ACTIVE SITE NEED CORRECT ENZYMES TO CLEAVE THE PRODRUG MOIETY AND RELEASE THE ACTIVE DRUG.

WE CAN AGREE THAT IF IT'S NOT GIVEN BY MEANS OF THE PRODRUG DELIVERY STRATEGY, THAT HURDLE DOESN'T APPLY?

A. YES, IF YOU IDENTIFY A DRUG THAT DOESN'T REQUIRE THAT, THAT'S FINE.

Q. I'D LIKE TO CULL UP EXHIBIT 2644. IT'S NOT YET BEEN ADMITTED INTO EVIDENCE.

THE COURT: OKAY.

THE WITNESS: I'M SORRY, WHICH?

BY MR. RABINOWITZ:

Q. EXHIBIT 2644. THEY'RE TABBED IN EXHIBIT NUMBER ORDER IN YOUR BINDER.

A. OKAY.

Q. AND THIS IS AN ARTICLE THAT YOU WROTE?

A. IT'S A REVIEW ARTICLE THAT I WROTE, YES.

MR. RABINOWITZ: YOUR HONOR, I MOVE THAT EXHIBIT 2644 BE ADMITTED.

MR. SINGER: NO OBJECTION, YOUR HONOR.

THE COURT: IT WILL BE ADMITTED.

(DEFENDANTS' EXHIBIT 2644 WAS RECEIVED IN EVIDENCE.)

BY MR. RABINOWITZ:

Q. THIS ARTICLE DISCUSSES FOSPHENYTOIN?

A. YES.

Q. AND THIS IS THE DRUG THAT YOU DISCUSSED YESTERDAY THAT WAS ADMINISTERED TO YOUR FORMER COLLEAGUE?

A. YES, YES. HIS DAUGHTER.

Q. A FORMER COLLEAGUE'S DAUGHTER. AND THAT WAS A GREAT MOMENT FOR YOU?

A. YES, IT WAS.

Q. NOW, IN THE ABSTRACT, IN THE SECOND LINE OF THE ABSTRACT YOU SAID FOSPHENYTOIN IS A PARENTERALLY USEFUL PRODRUG FORM OF PHENYTOIN? IS THAT CORRECT?

A. THAT'S THE FIRST SENTENCE, RIGHT.

Q. THE SECOND LINE. FOSPHENYTOIN IS A PARENTERALLY USEFUL

PRODRUG FORM OF PHENYTOIN. DID I READ THAT CORRECTLY?

A. YES. YES.

Q. AND WE CAN AGREED THAT FOSPHENYTOIN IS A PRODRUG OF PHENYTOIN?

A. YES.

Q. COULD I ASK YOU TO TURN TO PAGE 317 OF YOUR ARTICLE THAT'S MARKED IN THE EXHIBIT AS WITH THE LAST NUMBERS .0007 AT THE BOTTOM.

AND THERE'S A DIAGRAM AT THE BOTTOM THAT YOU DREW SHOWING HOW FOSPHENYTOIN WORKS TO DELIVER PHENYTOIN; IS THAT RIGHT?

A. YES. IT'S THE ETYMOLOGY OF THAT REACTION, YES.

Q. AND WE CAN AGREE IN YOUR DRAWING YOU SHOW HOW THE PRODRUG FOSPHENYTOIN GOES THROUGH AN INTERMEDIATE TO BECOME THE ACTIVE COMPOUND PHENYTOIN?

A. YES.

Q. AND THAT'S WHY WE KNOW THAT FOSPHENYTOIN IS A PRODRUG OF THE ACTIVE COMPOUND PHENYTOIN; CORRECT?

A. YES.

Q. CAN I ASK YOU TO LOOK AT EXHIBIT 2694. THIS IS NOT YET IN EVIDENCE. AND THAT'S ALSO IN YOUR BINDER.

DO YOU HAVE THAT, DR. STELLA?

A. YES.

Q. AND THIS IS A DRAWING THAT YOU PROVIDED IN YOUR EXPERT REPORT?

A. I BELIEVE SO, YES.

MR. RABINOWITZ: YOUR HONOR, WE MOVE THAT EXHIBIT 2694 BE ADMITTED IN EVIDENCE.

MR. SINGER: THERE IS NO OBJECTION, YOUR HONOR.

THE COURT: IT WILL BE ADMITTED.

(DEFENDANTS' EXHIBIT 2694 WAS RECEIVED IN EVIDENCE.)

BY MR. RABINOWITZ:

Q. DR. STELLA, WE CAN AGREE THIS SHOWS WHAT HAPPENS TO SOFOSBUVIR AFTER IT ENTERS THE BODY?

A. YES, THIS IS WHAT HAS BEEN, DR. SOFIA AND HIS COLLEAGUES, ET CETERA, HAS PROPOSED THIS IS WHAT GOES ON AND OTHERS.

Q. AND THIS IS HOW YOU ILLUSTRATE IT IN YOUR EXPERT REPORT?

A. YES.

Q. AND WE CAN AGREE THAT THE PRODRUG SOFOSBUVIR GOES THROUGH A NUMBER OF INTERMEDIATES TO BECOME THE ACTIVE COMPOUND WHICH IS DEPICTED AT THE BOTTOM LEFT?

A. YES.

Q. AND THAT'S CALLED GS-461203?

A. YES.

Q. AND IT'S ALSO CALLED PSI-7409?

A. THAT'S MY UNDERSTANDING.

Q. CAN I ASK YOU TO LOOK AT EXHIBIT 2648. THIS IS ANOTHER DRAWING THAT YOU PROVIDED IN YOUR EXPERT REPORT?

A. YES.

Q. AND WITH THE ASSOCIATED TEXT?

A. RIGHT.

MR. RABINOWITZ: YOUR HONOR, I MOVE THAT EXHIBIT 2648 BE ADMITTED INTO EVIDENCE.

MR. SINGER: THERE'S NO OBJECTION, YOUR HONOR.

THE COURT: IT WILL BE ADMITTED.

(DEFENDANTS' EXHIBIT 2648 WAS RECEIVED IN EVIDENCE.)

BY MR. RABINOWITZ:

Q. WE CAN AGREE GS-461203 IS THE TRIPHOSPHATE THAT IS THE ACTIVE FORM OF SOFOSBUVIR?

A. YES, THAT'S MY UNDERSTANDING.

Q. AND THIS TRIPHOSPHATE IS THE VIRUS STOPPER?

A. THAT IS MY UNDERSTANDING.

Q. DR. STELLA, I'D LIKE TO SHOW YOU A DEMONSTRATIVE THAT DR. SOFIA USED IN HIS TESTIMONY. CAN WE SHOW PDX-310?

A. IS THIS IN MY --

Q. IT IS NOT. WE'LL SHOW THAT TO YOU ON THE SCREEN.

A. OKAY.

Q. WE CAN AGREE THAT THIS IS THE STRUCTURE OF SOFOSBUVIR?

A. I BELIEVE THAT'S TRUE. I AGREE.

Q. WELL, IF YOU WOULD LIKE TO TAKE A LOOK. WE CAN LOOK AT WHAT IS ALREADY IN EVIDENCE IS 2602 IS THE SOFOSBUVIR LABEL THAT IS IN YOUR BINDER.

A. 2?

Q. 26 -- 2062, THE SOVALDI LABEL?

MR. SINGER: COUNSEL, WHAT PAGE?

MR. RABINOWITZ: 2062?

THE WITNESS: 2062. I THOUGHT YOU SAID 22. OKAY. GO AHEAD.

BY MR. RABINOWITZ:

Q. AND WOULD YOU LIKE TO TURN TO THE PAGE THAT ENDS AT THE BOTTOM OF 310. CAN YOU SHOW THE DEMONSTRATIVE, PLEASE. NOT THE LABEL, THE DEMONSTRATIVE FROM DR. SOFIA'S PDX-310?

A. YES.

Q. AND CAN YOU SATISFY YOURSELF NOW THAT THAT IS THE STRUCTURE OF SOFOSBUVIR?

A. YES.

Q. AND THIS DRUG CONSISTS OF A STRUCTURE PRODRUG MOIETY ON THE LEFT?

A. MULTIPLE PROMOIETIES ON THE LEFT.

Q. AND THE PRODRUG PART IS THE PART IN YELLOW THERE; CORRECT?

A. NO.

Q. AND WHERE IS THE PRODRUG PART? WOULD YOU DRAW IT, PLEASE.

A. CAN I DRAW ON THIS?

Q. YES, PLEASE DO. OKAY. SO LET'S GO BACK TO THE UNHIGHLIGHTED VERSION. SO THAT'S THE PRODRUG PART ON THE LEFT AND THERE'S A NUCLEOSIDE ON THE RIGHT?

A. SORRY. I DIDN'T REALIZE I DROPPED MY VOICE. THE PROMOIETY IS THE TWO AREAS THAT I'VE COVERED. WHAT IS LEFT IS THE NUCLEOTIDE.

Q. SO THE NUCLEOTIDE ANALOG IS IN RED AND THE PRODRUG PART IS IN YELLOW?

A. WRONG.
Q. WHICH IS THE NUCLEOTIDE PART?
A. IT INCLUDES THE PHOSPHATE.
Q. OKAY. THAT'S THE NUCLEOTIDE?
A. AND IT WOULD HAVE TO HAVE TWO OXYGENS ON THE PHOSPHOROUS.
Q. AND IN THE NUCLEOTIDE PORTION OF SOFOSBUVIR, THE SUGAR HAS A 2' METHYL IN THE UP POSITION AND A 2' FLUORO IN THE DOWN POSITION; CORRECT?
A. YES, YES, IT DOES.
Q. CAN YOU CALL UP EXHIBIT 1542 ON THE SCREEN.
AND IT'S IN YOUR BINDER, DR. STELLA, 1542. 1-5-4-2?
THIS IS THE MERCK/ISIS JOINT RESEARCH COMMITTEE REPORT DATED 18TH OF APRIL 2001. DO YOU HAVE THAT EXHIBIT?
A. YEP.
Q. AND PLEASE REFER TO THE PAGE MARKED AT THE BOTTOM AS PAGE 0056. DO YOU SEE THE STRUCTURE ON THE TOP LEFT?
A. HOLD ON. OKAY.
Q. DO YOU SEE THE STRUCTURE ON THE TOP LEFT?
A. YES.
Q. AND THE SUGAR IN THAT STRUCTURE HAS A 2' METHYL UP AND A 2' FLUORO DOWN?
A. YES.
Q. AND CAN WE AGREE -- WE CAN AGREE THAT THE SUGAR RING DEPICTED IN THIS STRUCTURE IS THE SAME AS THE SUGAR IN SOFOSBUVIR?

A. I DON'T KNOW WHETHER THESE WERE ACTUALLY MADE OR JUST PROPOSED COMPOUNDS. I DON'T KNOW ENOUGH ABOUT WHAT IS ON HERE. AND AS I SAID, THE BASE IS DIFFERENT, BUT I DON'T KNOW WHAT THE HISTORY OF THESE COMPOUNDS ARE, WHETHER THESE WERE ACTUALLY MADE, PROPOSED OR WHATEVER.

Q. AND COMPARING THE SUGAR RING THAT IS DEPICTED IN THIS STRUCTURE DRAWN HERE WITH THE SUGAR RING IN SOFOSBUVIR, THEY BOTH HAVE A METHYL UP AND A FLUORO DOWN; CORRECT?

A. ONLY CONSIDERING THE SUGAR, THAT IS CORRECT. I DON'T KNOW WHAT THE STEREOCHEMISTRY IS ON THE OTHER HYDROXYL BUT THE ONE ON THE 3 POSITION.

Q. AND YOU AGREE THAT SOFOSBUVIR IS A PHOSPHORAMIDATE PRODRUG?

A. AS THAT TERM IS USED, YES.

Q. AND THAT IS ALSO KNOWN AS MCGUIGAN PRODRUGS?

A. MCGUIGAN DID A LOT OF DIFFERENT PRODRUGS BUT THAT TERM HAS BEEN USED, YES.

Q. AND PROFESSOR MCGUIGAN HAS BEEN CREDITED WITH INVENTING PHOSPHORAMIDATE PRODRUGS?

A. YEAH, MCGUIGAN, I THINK HE'S THE ONE THAT IT'S BEEN ATTRIBUTED TO HIM.

Q. WOULD YOU PLEASE TURN TO EXHIBIT 0802.

A. 0?

Q. 0802. THIS IS AN INTERNATIONAL PATENT APPLICATION PUBLISHED AS WO 00/47591?

A. YES.
Q. AND ONE OF THE INVENTORS IS CHRISTOPHER MCGUIGAN?
A. YES.
Q. AND YOU KNOW WHO CHRISTOPHER MCGUIGAN IS?
A. I KNOW OF HIM. I DON'T KNOW HIM.
Q. HE'S ONE OF THE LEADERS IN THE AREA OF PRODRUGS?
A. NOT GENERALLY RECOGNIZED AS THAT, BUT HE'S RECOGNIZED AS MADE A MAJOR CONTRIBUTION TO PRODRUGS THROUGH HIS WORK, YES.
MR. RABINOWITZ: YOUR HONOR, I WOULD MOVE THAT THIS EXHIBIT BE ADMITTED INTO EVIDENCE.
MR. SINGER: THERE'S NO OBJECTION, YOUR HONOR.
THE COURT: IT WILL BE ADMITTED.
(DEFENDANTS' EXHIBIT 802 WAS RECEIVED IN EVIDENCE.)
BY MR. RABINOWITZ:
Q. WOULD YOU PLEASE TURN TO PAGE 9, NUMBER 9 AT THE TOP AND THE NUMBER AT THE TOP IS .0011?
DO YOU SEE THERE'S A STRUCTURAL FORMULA?
A. YES.
Q. AND WE CAN AGREE THAT THE STRUCTURAL FORMULA HAS A NUCLEOSIDE ON THE LEFT?
A. ARE YOU GOING TO HIGHLIGHT THE NUCLEOSIDE?
Q. WELL, JUST LET'S ESTABLISH THAT THERE'S -- THE LEFT PART IS THE NUCLEOSIDE?
A. FOR THE JURY, THIS IS THE NUCLEOSIDE HERE (INDICATING).
Q. AND THE STRUCTURAL FORM HAS A PRODRUG ON THE RIGHT?

A. WELL, ACTUALLY, THIS IS THE PRODRUG PART HERE, AND IT ALSO HAS A PHOSPHATE WHICH IS TO PRODUCE THE NUCLEOTIDE.

Q. AND THE TABLE BELOW GIVES A NUMBER OF EXAMPLES WITH DIFFERENT CHOICES THAT R1, R2, R3, R4, AND R5; CORRECT?

A. YES.

Q. AND I'D LIKE YOU TO COMPARE THE PRODRUG MOIETY IN MCGUIGAN'S EXAMPLE NUMBER 11 WITH THE PROMOIETY IN SOFOSBUVIR.

R1 IN THE MCGUIGAN EXAMPLE 11 IS PHENYL; CORRECT?

A. YES.

Q. AND WE CAN AGREE THAT'S THE SAME AS IN SOFOSBUVIR?

A. NUMBER 11 DID YOU SAY?

Q. NUMBER 11?

A. YES.

Q. R2 IN THE MCGUIGAN EXAMPLE NUMBER 11 IS HYDROGEN?

A. YES.

Q. AND THAT'S THE SAME AS IN SOFOSBUVIR?

A. YES.

Q. AND R3 IN MCGUIGAN EXAMPLE 11 IS METHYL?

A. I CAN GIVE AN ANSWER HERE THAT IS BOTH YES AND NO.

YES, IT'S A METHYL GROUP THAT IS IN BOTH OF THEM.

AS FAR AS I CAN TELL FROM THIS TABLE, IT DOESN'T DESIGNATE THE STEREOCHEMISTRY WHICH IS -- WHICH IN THE SOFOSBUVIR IS A SPECIFIC STEREOCHEMISTRY, UNLESS THERE'S SOMETHING ELSE IN THIS PATENT THAT SAYS THIS I DON'T -- THERE IS A METHYL GROUP THAT IS R3, BUT IT DOESN'T DESIGNATE THE STEREOCHEMISTRY.

Q. AND R3 IN SOFOSBUVIR IS METHYL AS WELL?
A. YES, BUT IT'S THE PARTICULAR STEREOCHEMISTRY OF THAT MATTER.
Q. ONE OF THE TWO PARTICULAR STEREOCHEMISTRY THAT ARE CONVEYED BY THIS DIAGRAM?
A. I DON'T KNOW IF THEY CONVEY THEM OR NOT, I DON'T KNOW.
Q. R4 IN THE MCGUIGAN EXAMPLE 11 IS O ISOPROPYL, O, I-S-O-P-R-O-P-Y-L?
A. THAT IS CORRECT.
Q. AND THE SAME IN SOFOSBUVIR?
A. YES, THERE'S ISOPROPYL.
Q. R5 IN MCGUIGAN EXAMPLE 11 IS HYDROGEN?
A. YES.
Q. AND SAME AS IN SOFOSBUVIR?
A. CORRECT.
Q. WOULD YOU AGREE THAT SOFOSBUVIR HAS THE SAME PRODRUG MOIETY THAT DR. MCGUIGAN DISCLOSED IN EXAMPLE 11?
A. IT DOES NOT.
Q. AND IF YOU LOOK AT THE TWO ALTERNATIVES STEREOCHEMISTRIES THAT FIT WITH EXAMPLE 11 IN MCGUIGAN, ONE OF THOSE TWO IS THE PRODRUG MOIETY IN SOFOSBUVIR?
A. IT DOES NOT.
Q. DR. STELLA, WOULD YOU TURN TO EXHIBIT 742. EXHIBIT 742, I BEG YOUR PARDON, EXHIBIT 742.
ARE YOU FAMILIAR WITH THIS DOCUMENT?

A. YEAH.
Q. AND THIS IS A PATENT THAT YOU OBTAINED FROM THE U.S. PATENT AND TRADEMARK OFFICE?
A. YES.
Q. AND YOU'RE THE FIRST NAMED INVENTOR?
A. YES.
MR. RABINOWITZ: YOUR HONOR, I WOULD MOVE THAT EXHIBIT 742 BE ADMITTED IN EVIDENCE.
MR. SINGER: THERE'S NO OBJECTION, YOUR HONOR.
THE COURT: IT WILL BE ADMITTED.
(DEFENDANTS' EXHIBIT 742 WAS RECEIVED IN EVIDENCE.)
BY MR. RABINOWITZ:
Q. THIS IS U.S. PATENT NUMBER 4,163,058; CORRECT?
A. YES.
Q. AND YOU ARE THE VALENTINO J. STELLA THAT IS LISTED AS THE FIRST NAMED INVENTOR?
A. YEAH. THERE ARE VERY FEW OF US AROUND, SO --
Q. AND SO I'D LIKE YOU TO TURN TO THE CLAIMS IN COLUMN 14, CLAIM 9.
CAN WE BLOW UP CLAIM 9, PLEASE.
CLAIM 9 IS A METHOD FOR ALLEVIATING CARDIAC ARRHYTHMIAS OR CONVULSIONS?
A. I'M SORRY. WHAT CLAIM IS IT?
Q. CLAIM 9.
A. 9. I THOUGHT YOU WERE ON CLAIM 1.

Q. AND CLAIM 9 IS DIRECTED TO A METHOD FOR TREATMENTS; CORRECT?

A. GIVE ME A MINUTE TO READ IT. I WANT TO MAKE SURE I GET IT RIGHT.

(PAUSE IN PROCEEDINGS.)

THE WITNESS: OKAY.

BY MR. RABINOWITZ:

Q. CLAIM 9 IS DIRECTED TO A METHOD FOR TREATMENT?

A. THAT'S WHAT IT APPEARS TO SAY, YES.

Q. AND TREATING CARDIAC ARRYTHMIA OR CONVULSIONS; CORRECT?

A. YES.

Q. BY ADMINISTERING ONE OF A CLASS OF COMPOUNDS DEFINED BY STRUCTURAL FORMULA?

A. THAT'S CORRECT.

Q. AND WE CAN AGREE THAT THIS PATENT CONTAINS NO DATA?

A. IT DOES NOT CONTAIN ANY DATA.

Q. YOU KNEW THIS PATENT HAD NO DATA WHEN YOU APPLIED FOR IT?

A. YES. WELL, WE HAD DATA, BUT IT JUST WASN'T INCLUDED -- I DIDN'T WRITE THE PATENT, SO I DID THE WORK AND A LAWYER PUT THIS TOGETHER AND WROTE THE PATENT.

Q. SO YOU HAD DATA WHEN YOU APPLIED FOR THIS PATENT, ALTHOUGH THE DATA DIDN'T APPEAR IN THE PATENT?

A. YEAH. I WAS NOT FAMILIAR WITH THE PATENTING PROCESS AT THAT TIME, SO I WAS PRETTY NAIVE AND THAT'S WHAT ENDED UP IN THE PATENT.

Q. AND THIS PATENT REPRESENTS THE FRUITS OF YOUR WORK THAT RESULTED IN THE DATA?

A. YES.

Q. AND YOU KNEW THE PATENT DIDN'T DISCLOSE THE DATA WHEN YOU OBTAIN IT?

A. I DIDN'T REALIZE THAT AT THAT TIME. I REALIZE IT NOW.

Q. AND YOU LICENSED THIS PATENT; CORRECT?

A. YES, IT WAS LICENSED TO MERCK.

Q. AND YOU MADE A MILLION DOLLARS OFF OF THIS PATENT?

A. I MADE A MILLION DOLLARS OFF OF THAT PATENT.

Q. AND YOU DIDN'T BELIEVE THIS PATENT WAS WORTHLESS WHEN YOU ACCEPTED A MILLION DOLLARS?

A. I'M SORRY?

Q. YOU DIDN'T BELIEVE THIS PATENT WAS WORTHLESS WHEN YOU ACCEPTED A MILLION DOLLARS FOR IT?

A. NO, I DID NOT. WE CAME OUT WITH A GREAT DRUG.

Q. AND YOU NEVER RETURNED THE MILLION DOLLARS TO MERCK THAT YOU OBTAINED FOR THIS PATENT?

A. WHY WOULD I?

MR. RABINOWITZ: NO FURTHER QUESTIONS.

THE COURT: REDIRECT FOR THIS WITNESS?

MR. SINGER: VERY BRIEFLY, YOUR HONOR.

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REDIRECT EXAMINATION

BY MR. SINGER:

Q. MR. ANG, IF WE CAN HAVE EXHIBIT 1542 AT PAGE 56.

DR. STELLA, YOU WERE POINTING TO THIS COMPOUND THAT I CIRCLED IN RED, AND I'LL CLEAR IT SO MR. ANG CAN HIGHLIGHT A LITTLE BIT BETTER THAN MY SCROLL.

YOU SAID THERE WAS A DIFFERENT BASE, BUT YOU DIDN'T SAY WHAT BASE WAS THERE. DOES THE A STAND FOR ADENOSINE? IS THAT CORRECT.

A. I BELIEVE SO.

Q. AND IS THAT A DOUBLE RING OR A SINGLE RING?

A. I BELIEVE IT'S A DOUBLE RING.

Q. THANK YOU. OKAY.

AND THE CLAIMS AT ISSUE HERE, THEY COVER DOUBLE RINGS OR SINGLE RINGS?

A. SINGLE RINGS.

Q. OKAY. AND WE CAN TAKE THAT DOWN. THANK YOU.

MR. RABINOWITZ WAS ASKING YOU SOME QUESTIONS ABOUT -- I REALLY ONLY HAVE ONE OTHER SET OF QUESTIONS FOR YOU -- ABOUT THE COLUMN 34, LINES 31 TO 37 IN THE PATENT.

A. IS THIS IN THE PATENT?

Q. YES, IN THE '499 PATENT.

AND, MR. ANG, IT WAS THE PART, YEAH, ABOUT THE RECTAL, TOPICAL, PARENTERAL, OCULAR, PULMONARY. DO YOU REMEMBER THOSE QUESTIONS?

A. YEAH.
Q. AND, DR. STELLA, FIRST OFF, ARE THERE ANY EXAMPLES IN THE PATENT OF PRODRUGS THAT ARE DELIVERED -- IF YOU CAN HIGHLIGHT THERE -- RECTALLY, TOPICALLY, PARENTERALLY, OCULARLY, PULMONARILY OR NASALLY, ARE THERE ANY EXAMPLES OF THAT IN THE PATENT?
A. NO, THERE'S NOT.
Q. AND IS THIS A LAUNDRY LIST OF POSSIBILITIES?
A. THAT'S A LAUNDRY LIST OF POSSIBILITIES.
Q. ARE THESE THINGS ENABLED BY THE PATENT-IN-SUIT?
A. ABSOLUTELY NOT.
Q. OKAY. YOU WENT THROUGH YOUR LITTLE HURDLE DIAGRAM, AND WE TALKED ABOUT ORAL, HOW IT WASN'T ENABLED FOR ORAL, SO I'M NOT GOING TO GO THROUGH THAT AGAIN.
COULD YOU HAVE LISTED A SIMILAR SET OF HURDLES FOR RECTAL DELIVERY, TOPICAL DELIVERY, PARENTERALLY DELIVERY, OCULAR DELIVERY, NASAL DELIVERY, AND PULMONARY HERE?
A. YES.
Q. WOULD WE HAVE BEEN ALL DAY HERE TODAY AND TOMORROW IF YOU HAD TO EXPLAIN THE HURDLES FOR THOSE?
A. WE WOULD TAKE AT LEAST ANOTHER TWO OR THREE OR FOUR HOURS.
Q. THANK YOU. I HAVE NO FURTHER QUESTIONS.
THE COURT: ANYTHING ELSE FOR THIS WITNESS, MR. RABINOWITZ?
MR. RABINOWITZ: NO, YOUR HONOR.

THE COURT: MAY DR. STELLA BE EXCUSED?

MR. RABINOWITZ: YES, YOUR HONOR.

THE COURT: THANK YOU, DR. STELLA. YOU ARE FREE TO STEP DOWN.

THE WITNESS: THANK YOU, YOUR HONOR.

THE COURT: YOU'RE ALSO FREE TO GO.

MS. BROOKS, YOUR NEXT WITNESS?

MS. BROOKS: YES, YOUR HONOR.

OUR NEXT WITNESS IS DR. JOHN SECRIST, AND IF WE CAN HAVE A MOMENT TO GET OUR BINDERS TO DISTRIBUTE?

THE COURT: OF COURSE.

THE CLERK: PLEASE RAISE YOUR RIGHT HAND.

(PLAINTIFF'S WITNESS, JOHN SECRIST, WAS SWORN.)

THE WITNESS: YES.

THE CLERK: THANK YOU, SIR. PLEASE BE SEATED.

AND IF YOU WOULD STATE YOUR NAME AND SPELL YOUR LAST NAME FOR THE RECORD.

THE WITNESS:

MS. BROOKS: YOUR HONOR, MAY I APPROACH WITH A BINDER FOR BOTH THE COURT AND DR. SECRIST.

THE WITNESS: JOHN S. SECRIST, III, S-E-C-R-I-S-T.

DIRECT EXAMINATION

BY MS. BROOKS:

Q. GOOD MORNING, DR. SECRIST.

A. GOOD MORNING.

Q. DR. SECRIST, ARE YOU HERE TO GIVE YOUR EXPERT OPINION AS A CHEMIST, AND SPECIFICALLY A MEDICINAL CHEMIST, ON WHETHER OR NOT THE ASSERTED CLAIMS IN THE '499 PATENT AND THE '712 PATENT ARE INVALID FOR LACK OF WRITTEN DESCRIPTION AND ENABLEMENT?

A. YES, I AM.

Q. SO BEFORE WE DO THAT, WE NEED TO QUALIFY YOU AS AN EXPERT TO MAKE SURE THAT YOU INDEED HAVE THE APPROPRIATE CREDENTIALS TO RENDER SUCH AN OPINION.

A. I UNDERSTAND.

Q. LET'S START, DR. SECRIST, WITH CAN YOU TELL THE LADIES AND GENTLEMEN OF THE JURY WHAT YOU ARE CURRENTLY DOING?

A. YES. I AM RETIRED. I'VE BEEN RETIRED OVER TWO YEARS NOW. I RETIRED FROM THE SOUTHERN RESEARCH INSTITUTE, WHICH WAS LOCATED IN BIRMINGHAM, ALABAMA.

SINCE BEING RETIRED, I'VE BEEN INVOLVED IN A NUMBER OF THINGS, AND I'LL CONTINUE TO BE INVOLVED IN A NUMBER OF THINGS. I HAVE DONE SOME CONSULTING WORK SINCE RETIRING. I CONTINUE TO EDIT A JOURNAL IN THE FIELD SINCE RETIRING, AND I'M STILL INVOLVED WITH SOUTHERN RESEARCH INSTITUTE IN SEVERAL WAYS.

ONE OF THOSE WAYS, WHICH IS REALLY EXCITING TO ME, IS WE ARE PUTTING TOGETHER A BOOK THAT I'LL SAY HIGHLIGHTS THE ACCOMPLISHMENTS OF SOUTHERN RESEARCH INSTITUTE OVER THE YEARS.

AND SO I GET TO WORK WITH A NUMBER OF COLLEAGUES WHO HAVE BEEN INVOLVED IN SOME REALLY EXCITING THINGS PUTTING TOGETHER INFORMATION FOR A LAY AUDIENCE DESCRIBING WHAT SOUTHERN

RESEARCH INSTITUTE HAS BEEN DOING, AND IT'S BEEN WORTHWHILE AND IT'S BEEN A SPECTACULAR AMOUNT OF STUFF, ALTHOUGH I IMAGINE NONE OF YOU HAVE NEVER HEARD OF SOUTHERN RESEARCH INSTITUTE.

THE SECOND THING I'M DOING FOR SOUTHERN RESEARCH INSTITUTE AFTER RETIRING IS HELPING THEM IN FUND RAISING.

Q. SO DOING FUND RAISING, IS SOUTHERN RESEARCH INSTITUTE A FOR PROFIT OR A NONPROFIT RESEARCH INSTITUTE?

A. IT'S A 5103, SO A NOT FOR PROFIT RESEARCH INSTITUTE THAT ENGAGED IN A VARIETY OF DIFFERENT KINDS OF RESEARCH.

Q. AND CAN YOU DESCRIBE FOR THE LADIES AND GENTLEMEN OF THE JURY WHAT SOUTHERN RESEARCH INSTITUTE DOES?

A. SURE. IT'S AN INDEPENDENT RESEARCH ORGANIZATION. WE HAVE THREE AREAS.

ONE OF THEM IS ONE THAT CONCERNS THESE PROCEEDINGS, THAT IS, LIFE SCIENCES. WE DO A LOT OF WORK WITH DRUG DISCOVERY, A LOT OF WORK WITH DRUG DEVELOPMENT, AND WE'VE BEEN DOING THAT FOR OVER 50 YEARS.

WE HAVE A SECOND ENTITY RELATED TO ENGINEERING. AND THOSE FOLKS DO A LOT OF THINGS.

AND BY THE WAY, THE WORK IN LIFE SCIENCES. THE VAST MAJORITY OF THEM HAVE BEEN FUNDED BY THE NATIONAL INSTITUTE OF HEALTH THROUGH GRANTS AND CONTRACTS.

IN THE ENGINEERING AREA, OUR WORK HAS COME MAINLY FROM NASA AND D.O.D. WE HAVE BEEN INSTRUMENTAL IN THE MAN SPACE PROGRAM SINCE ITS BEGINNING, AND WE HAVE DONE A LARGE AMOUNT OF

WORK ON MATERIALS THAT ARE USED FOR A VARIETY OF PURPOSES FOR NOT ONLY NASA, BUT D.O.D.

THE THIRD PIECE OF WHAT SOUTHERN RESEARCH INSTITUTE HAS DONE OVER THE YEARS IS IN THE ENVIRONMENTAL AREA. WE HAVE DONE A LOT OF WORK FOR EPA, FOR POWER COMPANIES RELATING TO AIR QUALITY.

AND IN THE LAST, I'LL SAY, FIVE YEARS -- TIME FLIES -- THE LAST FIVE YEARS WE'VE GOTTEN INVOLVED IN WATER QUALITY AS WELL.

SO THAT GIVES YOU, I THINK, A QUICK VIEW OF WHAT WE DO AND WHERE OUR MONEY COMES FROM. ALL OF THE MONEY COMES FROM OUTSIDE, SO WE HAVE TO ATTRACT MONEY BY PROPOSING TO DO WORTHWHILE THINGS FOR PEOPLE.

Q. AND HOW LONG WERE YOU WITH SOUTHERN RESEARCH INSTITUTE BEFORE YOU RETIRED?

A. I JOINED SOUTHERN RESEARCH INSTITUTE IN LATE 1979. SO I WAS THERE OVER 34 YEARS, I GUESS.

Q. AND WHERE IS IT LOCATED?

A. IT'S LOCATED IN BIRMINGHAM, ALABAMA. AND I HAD NEVER -- I'LL SAY I HAD NEVER BEEN IN ALABAMA BEFORE, AND VISITING THERE THE FIRST TIME -- I GUESS I COULD TALK ABOUT THAT IF YOU WISH.

Q. WELL, WHERE WERE YOU BEFORE YOU JOINED SOUTHERN RESEARCH INSTITUTE?

A. WELL, MAYBE I'LL JUST DESCRIBE SORT OF MY CHRONOLOGY LEADING UP TO THAT. IS THAT ALL RIGHT?

Q. PLEASE, YES.

A. SO I GOT A BACHELORS IN CHEMISTRY AT THE UNIVERSITY OF MICHIGAN MANY YEARS AGO.

THEN I WENT TO THE UNIVERSITY OF ILLINOIS FOR A PH.D. IN ORGANIC CHEMISTRY, AND YOU'LL RECALL THAT DR. SOFIA DID EXACTLY THE SAME THING. HE'S TEN YEARS YOUNGER THAN ME, SO WE DIDN'T OVERLAP.

BUT I WENT TO THE UNIVERSITY OF ILLINOIS FOR THE SAME REASON. IT WAS ONE OF THE TOP CHEMISTRY PROGRAMS IN THE COUNTRY AND I WANTED TO GO WHERE I COULD DO THE BEST. SO I GOT A PH.D. FROM THE UNIVERSITY OF ILLINOIS.

THEN I WAS LUCKY ENOUGH TO GET A POST-DOCTORAL FELLOWSHIP -- ACTUALLY I HAVE POST-DOCTORAL FELLOWSHIPS DOING MY PH.D. WORK, AND IN MY POST-DOC FROM THE NATIONAL INSTITUTE OF HEALTH, BOTH PLACES.

ANYHOW, I WENT TO HARVARD FOR A POST-DOCTORAL STAY WITH PROFESSOR E.J. COREY, ELIAS J. COREY. HE HAS A NOBEL PRIZE IN CHEMISTRY, AN OUTSTANDING GENTLEMAN AND AN OUTSTANDING SCIENTIST.

THEN I MOVED TO THE OHIO STATE UNIVERSITY. I WAS A FACULTY MEMBER THERE FOR SOME YEARS IN THE CHEMISTRY DEPARTMENT, AND I GUESS I WOULD SAY THAT AT THAT TIME FOR A YOUNG PERSON WHAT I WANTED TO DO WAS TO FOCUS ON DRUG DISCOVERY.

AND IT'S VERY HARD TO DO THAT, OR IT WAS AT THAT TIME AT THE UNIVERSITY, AND ESPECIALLY FOR A YOUNGER PERSON. SO I

WANTED TO MAKE A TRANSITION TO AN ORGANIZATION THAT WOULD ALLOW ME TO REALLY GET MEANINGFULLY INVOLVED IN DRUG DISCOVERY.

AND WHILE I WAS AT OHIO STATE, I HAD WON A RESEARCH CONTRACT WITH THE UNITED STATES ARMY, AND THE PURPOSE OF THIS CONTRACT WAS ACTUALLY TO MAKE NUCLEOSIDES -- BY THE WAY, MY PH.D. WAS IN NUCLEOSIDES AS WELL. SO I HAD BEEN WORKING WITH THE NUCLEOSIDE AREA SINCE 1968.

SO I HAD THIS SIGNIFICANT SIZE CONTRACT WITH THE ARMY TO MAKE ANTI-PARASITIC COMPOUNDS THAT WERE NUCLEOSIDES.

THE ARMY WOULD HAVE, ONCE A YEAR, A MEETING WITH ALL OF THE PEOPLE THEY HAD WORKING WITH MALARIA AND VARIOUS OTHER PARASITES AND EVERYBODY GOT TOGETHER AND TALKED ABOUT THEIR RESULTS.

I WENT TO THIS MEETING LESS THAN A YEAR AFTER I WAS AWARDED THIS CONTRACT AND MET ALL OF THE PEOPLE THERE.

AMONG THE FOLKS THERE WERE SOME PEOPLE FROM SOUTHERN RESEARCH INSTITUTE BECAUSE THEY WERE DOING A LOT OF THIS WORK IN THIS AREA AT THE TIME.

SO I MET ALL OF THEM. WE MADE PRESENTATIONS.

AND THE LEADER OF THAT GROUP AT SOUTHERN RESEARCH WAS ALSO SECOND IN COMMAND AT SOUTHERN RESEARCH, HE WAS VERY INTERESTED IN ME AND WONDERED IF I MIGHT WANT TO WORK AT THE SOUTHERN RESEARCH INSTITUTE IN BIRMINGHAM, ALABAMA.

AND I SAID, WELL, WHY DON'T I COME DOWN AND VISIT?

I DID THAT AND I VISITED ALABAMA AND I DISCOVERED THAT

THESE FOLKS HAVE -- HAD AT THE TIME, AND STILL HAVE, A SPECTACULAR DRUG DISCOVERY OPERATION. THEY DO WHAT YOU NEED TO DO TO ACTUALLY DISCOVER AND DEVELOP NEW DRUGS. THEY HAD A TEAM -- AND WE'VE TALKED ABOUT A TEAM ALL WEEK -- THEY HAD A TEAM TO DO IT AND YOU COULD SEE IT.

SO I WENT HOME, AND MY WIFE HAD ALSO NEVER BEEN TO ALABAMA AND I SAID, SAY, THIS LOOKS VERY GOOD. AND I REMEMBER HER RESPONSE FAIRLY CLEARLY. SHE SAID, ALABAMA?

AND SO WE TOOK HER DOWN TO ALABAMA ALSO AND SHE WAS TREATED I'LL SAY VERY NICELY. WE HAD YOUNG CHILDREN AT THE TIME. THEY WERE ALSO TREATED NICELY.

ANYHOW, WE CAME BACK AND SHE SAID WELL, OKAY, IT LOOKS LIKE A NICE PLACE AND THE SCHOOL SYSTEMS ARE REASONABLE. IF YOU WANT TO DO THAT, IT'S FINE WITH ME.

SO I SAID, WHY DON'T WE TRY IT FOR A FEW YEARS AND SEE IF I LIKE THE PLACE AND IF I CAN DO WHAT I WANT TO DO? BECAUSE IT'S A PLACE WHERE YOU HAVE TO USE YOUR OWN IDEAS AND THEY DON'T TELL YOU WHAT TO DO. YOU USE YOUR OWN IDEAS AND YOU GET MONEY TO DO IT AND THEN YOU DO IT.

SO WE MOVED TO ALABAMA THINKING WE'LL BE HERE FOR A FEW YEARS AND SEE WHERE WE GO, AND AS YOU'VE HEARD, I'VE STAYED THERE OVER 34 YEARS.

Q. AND WHAT PERCENTAGE OF YOUR CAREER HAS BEEN FOCUSSED SPECIFICALLY ON DRUG DISCOVERY IN THE AREA OF NUCLEOTIDES AND NUCLEOSIDES?

A. WELL, MY PH.D. WORK WAS IN THE AREA OF NUCLEOSIDES.

I WOULD SAY ONLY, ONLY PARTIALLY FOCUSSED IN DRUG DISCOVERY. WITH PROFESSOR COREY AT HARVARD, I WAS NOT INVOLVED IN NUCLEOSIDES AT ALL.

WHEN I JOINED OHIO STATE, FROM THAT POINT UNTIL NOW I'VE BEEN INVOLVED IN NUCLEOSIDE DRUG DISCOVERY. SO I WOULD SAY, I DON'T KNOW, 95 PERCENT OR SOMETHING LIKE THAT.

Q. HAVE YOU EVER BEEN INVOLVED IN ANY TYPE OF DRUG DISCOVERY WORK WHERE YOU SCREENED NUCLEOSIDES AND OTHER COMPOUNDS FOR BIOLOGICAL ACTIVITY?

A. OH, YES, OF COURSE.

WELL, ALL OF OUR GRANTS OVER THE YEARS THAT CAME FROM, MOSTLY FROM NIH, BUT ALSO FROM OTHER ORGANIZATIONS, ALL OF THEM INVOLVED MAKING NUCLEOSIDES AND EVALUATING THEM FOR WHATEVER PURPOSE IT MIGHT HAVE BEEN. IT COULD HAVE BEEN AN ANTI-VIRAL PURPOSE. IT COULD HAVE BEEN AN ANTI-CANCER PURPOSE. IT COULD HAVE BEEN OTHER THINGS.

WE HAD, HOWEVER, ONE INTERESTING PROJECT. THAT WAS AN NIH CONTRACT WHEREBY I WAS THE PRINCIPAL INVESTIGATOR OF THIS CONTRACT AND THERE WERE -- I THINK I HAD FOUR OTHER PH.D. CHEMISTS THAT WERE INVOLVED WITH ME.

OUR JOB WAS TO GO OUT ACROSS THE WORLD TO VARIOUS CHEMISTRY LABS AND TRY TO CONVINCE CHEMISTS TO SEND IN COMPOUNDS TO NIH.

THESE COMPOUNDS THEN WOULD BE EVALUATED FOR THEIR

ANTI-VIRAL ACTIVITY AGAINST UP TO ABOUT 27 DIFFERENT VIRUSES. ANY GIVEN COMPOUND MIGHT NOT HAVE BEEN DONE AGAINST ALL 27, BUT ALL 27 WERE POSSIBLE.

AND WE PLAYED A ROLE IN DECIDING, WELL, WHICH COMPOUNDS MIGHT BE GOOD FOR WHICH VIRUSES AND HAVE THEM EVALUATED.

SO NIH WAS WILLING TO EVALUATE THESE COMPOUNDS AT NO COST TO ANY OF THE CHEMISTS ACROSS THE WORLD, WHICH THEY DID.

THE WAY THEY DID THAT WAS THROUGH A SERIES OF, I DON'T KNOW, SEVEN OR EIGHT OTHER CONTRACTS WITH BIOLOGICAL LABS.

DR. SEEGER, WHO YOU MET YESTERDAY, HE'S AN EXAMPLE OF A LAB WHO WOULD DO ANTI-VIRAL TESTING. HE'S NOT INVOLVED IN THIS PARTICULAR PROGRAM, BUT THERE ARE LABS THAT DO THAT AND THEY HAVE SPECIALTY, AND HIS SPECIALTY WAS HBV AND HCV. THOSE WERE TWO OF THE 27 VIRUSES.

AND THERE WERE TWO LABS AROUND THE COUNTRY THAT ACTUALLY LOOKED AT THOSE COMPOUNDS. ONE OF THEM TURNED OUT TO BE SOUTHERN RESEARCH INSTITUTE. SORRY.

OTHERS DID HERPES VIRUSES OR DID INFLUENZA OR, AS YOU MIGHT IMAGINE WITH 27 DIFFERENT VIRUSES, OR THEREABOUTS, YOU NEEDED A LOT OF DIFFERENT EXPERTISE TO DO THAT, SO A NUMBER OF LABS WERE INVOLVED.

OKAY. THE COMPOUNDS -- AND WE BROUGHT IN THOUSANDS AND THOUSANDS OF COMPOUNDS FROM ALL AROUND THE WORLD.

AND WE HELPED FOLKS GET THROUGH THE PROCESS, GET THE COMPOUNDS TO THE LAB AND SELECT THE VIRUSES TO BE SCREENED, AND

THEN THE LABS WOULD SEND US BACK THE BIOLOGICAL ACTIVITY.

SO WE WOULD, AS A MEDICINAL CHEMIST, ALL OF THE MEDICINAL CHEMISTS, WE WOULD EVALUATE THE BIOLOGICAL ACTIVITY, TRANSMIT IT TO THE CHEMISTS AROUND THE WORLD, AND THEN WORK WITH THEM TO DECIDE WHAT MIGHT BE DONE NEXT, IF ANYTHING.

SO A LOT OF CHOICES, SOMETIMES NOBODY HAD -- SOMEBODY WOULD HAVE NO COMPOUNDS IN INTEREST AND WE WOULD SAY, SORRY.

SOMETIMES THERE WERE COMPOUNDS OF INTEREST AND WE WOULD SAY, OKAY, YOU HAVE SOMETHING THAT MIGHT BE OF INTEREST HERE. DO YOU HAVE ANY OTHER COMPOUNDS LIKE THIS IN YOUR COLLECTION THAT WE CAN TEST? OR IF YOU DON'T, WOULD YOU BE INTERESTED IN MAKING SOME MORE OR COULD YOU MAKE SOME MORE COMPOUNDS SO THAT WE COULD TEST THOSE?

SO WE, WE WOULD HAVE A DIALOGUE WITH THE CHEMISTS FROM AROUND THE WORLD THAT MIGHT HELP THEM DECIDE WHAT THEY COULD DO NEXT. THAT COULD BE DONE THROUGH NIH AS WELL OR BY SOME OTHER MEANS IF THEY WISH, AND IT WAS ENTIRELY THEIR CHOICE.

AND WE WOULD ALSO HELP THEM -- IF THEY DECIDED THEY WANTED TO PUBLISH SOMETHING THAT CAME OUT OF THIS PROGRAM, WE WOULD MAKE SURE THAT THEY GOT THE DATA RIGHT AND EVERYTHING WAS SET.

BECAUSE A LOT OF CHEMISTS ARE NOT EXPERTS AT PUTTING BIOLOGICAL PROPERTY INTO A MANUSCRIPT FOR PUBLICATION AND WE DID ALL PHASES OF THIS, AND AS I SAID, WE EVALUATED, THROUGH THIS PROGRAM, THOUSANDS, TENS OF THOUSANDS OF COMPOUNDS AT A TIME WHEN IT WAS NOT DONE BY HIGH FREQUENCY SCREENING, WHICH

YOU HEARD ABOUT A LITTLE BIT EARLIER IN THE YEAR, OR EARLIER IN THE WEEK I MEAN, AND BY SORT OF NORMAL MEANS.

SO IT WAS A WAY THAT NIH WAS LOOKING FOR NEW ANTI-VIRAL DRUGS AGAINST A WIDE VARIETY OF VIRUSES. IT WAS A VERY WORTHWHILE PROGRAM.

Q. DR. SECRIST, COULD YOU HAVE MOVED FORWARD ON ANY OF THESE COMPOUNDS WITHOUT KNOWING IF THOSE COMPOUNDS HAD BIOLOGICAL ACTIVITY?

A. OH, OF COURSE NOT. OF COURSE NOT.

Q. THE PROJECT WOULD HAVE COME TO A SCREECHING HALT?

A. WELL, ONCE AGAIN, THERE WAS NO ACTIVITY. WE TOLD THE CHEMIST THERE WAS NO ACTIVITY AND WE MOVED ON.

Q. AND WHAT ROLE DID YOU PLAY, IF YOU COULD BRIEFLY TELL THE JURY, WHAT ROLE DID YOU PLAY IN THIS MASSIVE SCREENING PROJECT?

A. YEAH, I MENTIONED EARLIER I WAS THE PRINCIPAL INVESTIGATOR, SO I WAS THE PERSON THAT WAS OVERSEEING EVERYTHING THAT WENT ON IN THIS PROGRAM, AIL CONNECTION WITH THE CHEMIST, THE CONNECTION WITH THE BIOLOGICAL LABS, AND THE CONNECTION WITH THE GOVERNMENT BECAUSE THE GOVERNMENT WAS ALSO VERY INTERESTED IN THIS.

Q. DO YOU BELONG TO ANY PROFESSIONAL SOCIETIES IN THE FIELD OF NUCLEOSIDE DRUG DISCOVERY?

A. YES, I DO. THESE ARE GOING TO BE LONG NAMES.

THE PRINCIPAL SOCIETY THAT I'LL SAY NUCLEOSIDE AND NUCLEOTIDE CHEMISTS BELONG TO IS CALLED THE INTERNATIONAL

SOCIETY FOR NUCLEOSIDES, NUCLEOTIDES, AND NUCLEIC ACIDS.

THAT IS A SOCIETY THAT WAS FORMED, I'M NOT SURE, I'M GOING TO SAY 1990. I WAS ONE OF THE FIVE FOUNDERS OF THAT SOCIETY BACK IN WHATEVER YEAR THAT WAS.

Q. AND -- I'M SORRY, DR. SECRIST. AND DO THEY ACTUALLY -- ARE THERE ACTUALLY MEETINGS OF THIS INTERNATIONAL SOCIETY FOR NUCLEOTIDES AND NUCLEOSIDES AND NUCLEIC ACIDS?

A. OH, YES, THERE'S A MEETING EVERY YEAR. THIS YEAR IT'S IN PARIS. IT'S BEEN IN FRANCE BEFORE.

BUT, YES, IT'S EVERY OTHER YEAR. AND IT'S A GREAT WAY TO GET TOGETHER WITH PEOPLE WHO ARE DOING ALL KINDS OF NEAT THINGS IN THE NUCLEOTIDE AND NUCLEOSIDE AREA TO TALK ABOUT WHAT IS GOING ON AND PRESENT YOUR RESULTS AND SO FORTH.

SO IT'S A WONDERFUL SOCIETY THAT HAS PROSPERED OVER THE YEARS BECAUSE IT'S USEFUL.

Q. DO THEY GET PRETTY WILD AND CRAZY?

A. NO, OF COURSE NOT. ABSOLUTELY NOT.

Q. AND WHAT IS -- WHAT IS YOUR ROLE IN THAT SOCIETY?

A. WELL, OF COURSE, I WAS A FOUNDER AS I SAID, AND I WAS ELECTED THE PRESIDENT OF THAT SOCIETY FAIRLY EARLY ON. SO I SPENT TWO YEARS BEING THE PRESIDENT OF THE SOCIETY, AND I WAS INVOLVED AND ACTUALLY I CONTINUE TO BE INVOLVED IN THE AFFAIRS OF THE SOCIETY FROM ITS INCEPTION UNTIL NOW STILL.

Q. IS THERE A SECOND SOCIETY THAT YOU'RE INVOLVED IN THAT FOCUSES PRIMARILY ON NUCLEOSIDES AND NUCLEOTIDES?

A. WELL, THE OTHER ONE I WOULD MENTION IS THE INTERNATIONAL SOCIETY FOR ANTI-VIRAL RESEARCH.

THAT FOCUSES ON -- IT WAS A SOCIETY FORMED BY A SMALL GROUP OF VIROLOGISTS TO FOCUSES ON ANTI-VIRAL DRUG DISCOVERY AND DEVELOPMENT AND THAT'S REALLY WHAT IT WAS ABOUT.

AND CHEMISTS BEGAN GOING TO THE MEETINGS EARLY ON AND ALL OF A SUDDEN THERE WERE A LOT OF CHEMISTS AT THIS MEETING AND LOTS OF VIROLOGISTS.

SO IT WAS A GREAT WAY TO INTERFACE WITH PEOPLE IN THE ANTI-VIRAL DRUG DISCOVERY DEVELOPMENT ARENA, AND SO I PRETTY MUCH ATTENDED EVERY MEETING UNTIL MY RESPONSIBILITIES AT SOUTHERN RESEARCH CHANGED.

AND I WAS ALSO ELECTED PRESIDENT OF THAT INTERNATIONAL SOCIETY, AND IN THAT CASE I SPENT TWO YEARS AS THE INCOMING PRESIDENT AND TWO YEARS AS PRESIDENT AND TWO YEARS AS A PAST PRESIDENT. SO IT'S A SIX YEAR COMMITMENT.

BEFORE THAT I WAS ACTUALLY ELECTED TO BE THE TREASURER OF THAT SOCIETY, SO I SPENT SIX OR EIGHT YEARS OF THAT SOCIETY AS THE TREASURER.

SO, AGAIN, I'M STILL INVOLVED IN THE GOVERNANCE OF THAT SOCIETY NOW ALSO.

Q. HAVE YOU EVER EDITED ANY JOURNALS IN THE FIELD OF NUCLEOTIDES RESEARCH?

A. YES. I'M STILL CONTINUING WITH EDITING RESPONSIBILITIES. THE JOURNAL NUCLEOTIDES, NUCLEOSIDES, AND NUCLEIC ACIDS WAS

ESTABLISHED IN 1982 AND I WAS THE EXECUTIVE EDITOR AT THE TIME OF ITS IN EXCEPTION IN 1982, AND I'M STILL THE EXECUTIVE EDITOR OF IT TODAY.

Q. HAVE YOU PUBLISHED IN THE AREA OF NUCLEOSIDE COMPOUNDS AS DRUGS?

A. YES. OH, YES. AND I HAVE, I DON'T KNOW, 170, 180 PUBLICATIONS, SOMEWHERE IN THERE. MOST OF THOSE RELATE TO NUCLEOSIDES, NUCLEOTIDES, THOSE SORTS OF COMPOUNDS.

Q. HAVE YOU APPLIED FOR AND RECEIVED ANY UNITED STATES PATENTS?

A. YES, I HAVE. I THINK SOMEWHERE AROUND 40. I DON'T KNOW THE EXACT NUMBER. MAYBE CLOSE TO 40, MAYBE A LITTLE MORE.

SO, YES, I HAVE A NUMBER OF PATENTS THAT HAVE MY NAME ON THEM.

Q. AND DO ANY OF THEM RELATE TO NUCLEOSIDES?

A. I WOULD SAY MANY OF THEM DO. I DON'T KNOW THE NUMBER, BUT CERTAINLY WELL OVER HALF. MAYBE, MAYBE THREE-QUARTERS, MAYBE MORE. I'M NOT SURE. YES, THEY DO.

Q. HAVE YOU EVER INVENTED ANY DRUGS THAT HAVE BEEN APPROVED BY THE FOOD AND DRUG ADMINISTRATION?

A. YES, I HAVE. I GUESS AS A, AS A MEDICINAL CHEMIST -- AND WE HEARD THIS FROM DR. SOFIA -- THAT'S WHY YOU BECAME A MEDICINAL CHEMIST IS TO HELP WITH SOMETHING THAT MIGHT ACTUALLY MAKE A DIFFERENCE IN HUMAN HEALTH.

SO I'VE BEEN WORKING ALL OF THESE YEARS IN THE NUCLEOSIDE

FIELD LOOKING FOR DRUGS.

A LOT OF IT WAS ANTI-CANCER DRUGS AND WE CO -- ANOTHER SENIOR PERSON THAT DID RESEARCH ON IT CO-AMENDED A DRUG THAT DID BECOME FDA APPROVED CALLED CLOFARABINE.

Q. CLOFARABINE, C-L-O -- YOU DO IT. IT'S YOUR DRUG.

A. I KNOW HOW TO SPELL THIS DRUG. C-L-O-F-A-R-A-B-I-N-E.

Q. SO, DR. SECRIST, WE HEARD FROM DR. SOFIA A MOMENT THAT HE HAD IN TIME AT THE -- WHEN SOFOSBUVIR WAS APPROVED, AND WE HEARD FROM DR. STELLA A COUPLE OF STORIES ABOUT WHAT HAPPENED WITH HIM WHEN HIS DRUG WAS APPROVED.

CAN YOU TELL THE LADIES AND GENTLEMEN OF THE JURY WHAT HAPPENED WITH YOU WHEN YOUR DRUG WAS AT THE FDA APPROVAL HEARING, WHAT HAPPENED?

A. I'LL TRY. OKAY. FIRST OF ALL, CLOFARABINE IS A NUCLEOSIDE DRUG. IT HAS A DOUBLE RING BASE ON IT, AN ADENINE. IT'S A SUBSTITUTED ADENINE BASE -- SORRY -- IT HAS A SUBSTITUENT ON IT IN ADDITION TO THE NORMAL SUBSTITUENT.

THE SUGAR RING DOES HAVE A FLUORINE AT THE 2' POSITION AS WELL.

SO IT WAS A DRUG THAT WE PUSHED AS FAR AS WE COULD AT SOUTHERN RESEARCH, AND THEN WE LICENSED IT TO AN ORGANIZATION TO CARRY IT FURTHER, A SMALL COMPANY. LARGE COMPANIES WERE NOT INTERESTED IN THE DRUG. THEY DIDN'T THINK IT WOULD ACTUALLY BE WORTH ANYTHING.

SO WE LICENSED IT TO A SMALL COMPANY THAT WAS COMMITTED TO

IT, AND WE GOT SOME CLINICIANS WHO WERE VERY INTERESTED IN TESTING IT IN PATIENTS.

SO THE GROUP THAT WE WORKED WITH DURING THOSE YEARS AND REALLY HAD A WONDERFUL RELATIONSHIP WITH WAS AT M.D. ANDERSON CANCER CENTER IN HOUSTON, WHICH IS WORLD RENOWNED, AND PEOPLE COME THERE FOR CANCER TREATMENT FROM ALL OVER THE WORLD.

THE PEOPLE THAT WE WORKED WITH WERE EXPERIMENTS IN LEUKEMIA MAINLY, AND THIS DRUG WAS GOING TO BE LOOKED AT AS A POTENTIAL LEUKEMIA DRUG. AND THERE'S NO WAY TO KNOW WHEN YOU START CLINICAL TRIALS IN THE CANCER ARENA, WHAT CANCERS YOU MIGHT ACTUALLY BE ABLE TO HELP PEOPLE WITH, YOU CAN'T KNOW. YOU HAVE TO TRY TO FIND OUT.

SO YOU SAW FROM DR. MCHUTCHISON EARLIER IN THE WEEK THIS SLIDE WHERE HE TALKED ABOUT, WELL, YOU MAKE A POTENTIAL DRUG AND IT GOES INTO A PHASE 1 TRIAL AND PHASE 2 AND SO FORTH AND YOU SAW THAT.

WELL, WHAT WE COULD AFFORD, WHAT M.D. ANDERSON COULD DO TO HELP US OUT WITH WAS THE PHASE 1 TRIAL ON THIS DRUG. AND THEY DID THE PHASE 1 TRIAL, AND IT IS A SAFETY TRIAL. WILL THIS DRUG BE SAFE FOR PEOPLE TO TAKE?

SOMETIMES IN A SAFETY TRIAL YOU DO SEE SOME PEOPLE WHO WILL BE HELPED BY A DRUG. BUT YOU START OF COURSE WITH A VERY LOW DOSE AS WAS MENTIONED EARLIER AND YOU CAN MOVE UP.

ANYHOW, THE TRIAL WAS STARTED AT M.D. ANDERSON WITH CLOFARABINE IN ADULTS WITH LEUKEMIA. IT COULD BE WHATEVER

KIND. AND THAT WAS ONGOING WHEN ONE OF THE -- ACTUALLY A PARENT OF A PATIENT AT M.D. ANDERSON.

BY THE WAY, I DIDN'T MENTION THIS, CLOFARABINE WAS APPROVED BY FDA FOR CHILDHOOD LEUKEMIA. IT WAS ACTUALLY USED ROUTINELY IN ADULT LEUKEMIA AND IT WORKS BEAUTIFULLY THERE. BUT IT WAS INITIALLY APPROVED BY THE FDA FOR CHILDHOOD LEUKEMIA.

HOW DID THAT COME ABOUT? THERE WAS A COUPLE OF FOLKS, PARENTS WERE THERE WITH THEIR SON AT M.D. ANDERSON AND THEIR SON HAD GONE THROUGH ALL OF THE TREATMENTS THAT THEY HAD AND THERE WAS NOTHING LEFT AND IT DIDN'T WORK.

SO YOU CAN PUT YOURSELF --

Q. SORRY, DR. SECRIST. WAS HE CURED?

A. YES.

Q. FIVE YEARS OLD?

A. OR LESS.

Q. THANKS TO YOUR WORK.

A. I'M SORRY.

Q. AND --

A. ANYHOW, THE BOY CAME -- THE YOUNG LAD AND HIS DAD CAME TO THE APPROVAL HEARING FOR FDA. SO HE -- I GOT TO SEE HIM AT THIS APPROVAL HEARING.

THAT'S WHY YOU'RE A MEDICINAL CHEMIST.

Q. THANK YOU, DR. SECRIST.

YOUR HONOR, WE WOULD TENDER DR. SECRIST AS AN EXPERT IN

THE FIELD OF MEDICINAL CHEMISTRY, NUCLEOSIDE CHEMISTRY, AND NUCLEOSIDE DRUG DISCOVERY.

THE COURT: ANY OBJECTION?

MR. GENDERSON: NO OBJECTION, YOUR HONOR.

THE COURT: THE DOCTOR MAY SO TESTIFY.

BY MS. BROOKS:

Q. AND DO YOU HAVE SOME WATER UP THERE?

A. I DO.

AND I HAVE TO SAY, I DON'T THINK I MENTIONED THAT -- AT SOUTHERN RESEARCH I SAID I GOT A LITTLE BIT AWAY FROM RESEARCH BECAUSE THE LAST SEVEN YEARS I WAS THERE I WAS THE CEO AND PRESIDENT OF SOUTHERN RESEARCH, SO WHEN I RETIRED I WAS IN CHARGE OF THE ORGANIZATION.

SORRY, I LEFT THAT OUT.

Q. LET'S TURN NOW TO THE ANALYSIS THAT YOU DID IN THIS CASE OF THE '499 AND THE '712 PATENTS TO DETERMINE WHETHER OR NOT, IN YOUR EXPERT OPINION, THE ASSERTED CLAIMS ARE VALID OR INVALID.

NOW, FIRST, WHEN YOU FORMED YOUR OPINIONS, ARE YOU REQUIRED TO DO YOUR ANALYSIS FROM THE PERSPECTIVE OF WHAT IS CALLED A PERSON OF ORDINARY SKILL IN THE ART?

A. YES.

Q. AND, MR. ANG, IF WE CAN PULL UP PDX 702.

WE SAW A SIMILAR SLIDE TO THIS WITH DR. SEEGER AND AGAIN WITH DR. STELLA, AND WE WON'T READ THE ENTIRE SLIDE, BUT JUST

SO IT'S CLEAR FOR THE RECORD -- AND THIS IS PDX-702 -- THIS IS THE DEFINITION, OR AT LEAST GILEAD'S DEFINITION, OF WHAT ONE OF ORDINARY SKILL IN THE ART WOULD BE.

DID YOU KEEP THIS IN MIND AS YOU DID YOUR ANALYSIS?

A. YES, I DID.

Q. NOW, YOU YOURSELF ARE ONE OF EXTRAORDINARY SKILL IN THE ART I ASSUME?

A. I'LL GO ALONG WITH DR. STELLA'S STATEMENT IN THAT REGARD.

Q. SO HOW IS IT THAT YOU KNOW SO MUCH MORE THAN ONE OF ORDINARY SKILL IN THE ART, WHICH, BY THE WAY, IS IMPRESSIVE AS IT IS? HOW DO YOU DO YOUR ANALYSIS AND HOW DO YOU SET ASIDE THAT EXTRA LEARNING THAT YOU HAVE TO PUT YOURSELF IN THE SHOES OF ONE OF ORDINARY SKILL IN THE ART?

A. WELL, IN MY CASE, AS I SAID, I DID SPEND TIME AT OHIO STATE AND I DID HAVE A NUMBER OF PH.D. STUDENTS THERE. SO A NUMBER HAD PH.D. DEGREES OR MASTERS DEGREES WHILE I WAS THERE, SO I WAS WITH THEM IN THE LAB EVERY DAY AS THEY LEARNED CHEMISTRY AND BECAME, I WOULD SAY, GRADUATE PERSONS OF ORDINARY SKILL IN THE ART AND THEN BEYOND THAT.

IN ADDITION, MY MANY YEARS AT SOUTHERN RESEARCH, IT'S BEEN THE SAME. I'VE HAD MANY POST-DOCTORAL PEOPLE AT SOUTHERN RESEARCH WHO WORKED ON GRANTS, WE'VE HAD BACHELORS DEGREE CHEMISTS, MASTERS CHEMISTS AND PERMANENT STAFF THAT WORKED AT SOUTHERN RESEARCH THAT ALSO WORKED FOR ME.

SO IT'S -- I THINK IT'S EASY FOR ME TO PUT MYSELF IN THE

SHOES OF A PERSON OF ORDINARY SKILL.

Q. NOW, DOES MERCK HAVE A SLIGHTLY DIFFERENT DEFINITION OF THE QUALIFICATIONS OF A PERSON OF ORDINARY SKILL IN THE ORDER?

A. I READ THE MERCK DEFINITION AS WELL AS THIS ONE AND, YES, IT'S SLIGHTLY DIFFERENT.

Q. AND WOULD YOUR OPINIONS BE THE SAME WHETHER YOU DID YOUR ANALYSIS USING GILEAD'S DEFINITION OF ONE OF ORDINARY SKILL OR MERCK'S DEFINITION?

A. THEY WERE SUBSTANTIALLY THE SAME AND IT WOULDN'T MATTER RELATIVE TO MY OPINIONS.

Q. ALL RIGHT. LET'S NOW START BY SUMMARIZING YOUR OPINIONS AND THEN WE'LL GO BACKWARD AND SEE WHAT THE BASIS OF THOSE OPINIONS ARE.

MR. ANG, IF WE CAN GO TO PDX 701.

AND, DR. SECRIST, IF YOU COULD JUST WALK THE JURY THROUGH WHAT YOUR OPINIONS, YOUR ULTIMATE OPINIONS ARE IN THIS CASE?

A. YES.

ON THE LEFT YOU SEE THE SHORTENED SUMMARY. ON THE RIGHT YOU SEE A LITTLE MORE DETAIL.

AND WE HAVE BROKEN THEM OUT IN SEVERAL DIFFERENT WAYS.

BUT BASICALLY CLAIMS 1 AND 2 OF THE '499 PATENT, IN MY JUDGMENT THERE'S NO WRITTEN DESCRIPTION SUPPORT FOR THOSE CLAIMED METHODS AND THERE'S NO DISCLOSURE OF HOW TO MAKE AND USE THE METHODS WITHIN THE '499 PATENT.

IN THE '712 PATENT, CLAIMS 1 THROUGH 3, 5 AND 7, THE SAME

IS TRUE. THERE'S NO WRITTEN DESCRIPTION SUPPORT FOR ANY OF THOSE CLAIMED COMPOUNDS. AND THERE'S NO DISCLOSURE OF HOW TO MAKE AND USE THE CLAIMED COMPOUNDS.

IN FOR CLAIMS 9 THROUGH 11, IT'S SIMILARLY TRUE. THERE'S NO WRITTEN DESCRIPTION SUPPORT FOR THOSE CLAIMED COMPOUNDS, AND CERTAINLY NO DISCLOSURE OF HOW TO MAKE AND USE THOSE CLAIMED COMPOUNDS.

SO THE SUMMARY OVERALL IS ALL OF THESE CLAIMS ARE INVALID BASED OF LACK OF WRITTEN DESCRIPTION AND LACK OF ENABLEMENT.

Q. NOW, DR. SECRIST, YOU BROKE OUT SOME OF THE CLAIMS IN THE '712 PATENT. IN THE SECOND BULLET POINT YOU HAVE CLAIMS 1 THROUGH 3, 5 AND 7, AND IN THE THIRD BULLET POINT YOU HAVE CLAIMS 9 THROUGH 11.

WHY DID YOU BREAK THOSE OUT?

A. WELL, THE CLAIMS 9 THROUGH 11 ARE MUCH NARROWER IN SCOPE THAN THE VERY, VERY BROAD CLAIMS 1 THROUGH 3 AND THE VERY BROAD CLAIMS 5 THROUGH 7.

SO TO DISTINGUISH BETWEEN THE CLAIMS THAT WERE ABSOLUTELY MASSIVE AND CLAIMS THAT WERE MUCH NARROWER, I BROKE THEM OUT.

BUT THE INVALIDITY REASONS REMAIN THE SAME.

Q. ALL RIGHT. THEN LET'S TURN TO THE TWO PATENTS AT ISSUE. I'M GOING TO GET MY COPY HERE THAT I THINK MR. SINGER HAD BORROWED.

OH, IT'S RIGHT UP HERE. I BROUGHT IT WITH ME. OR I THOUGHT I DID.

IT'S IN YOUR BINDER FOR SURE.

SO IF WE LOOK AT EXHIBIT 1 IN YOUR BINDER, DR. SECRIST, IT'S ALREADY IN EVIDENCE.

A. YES.

Q. THAT'S THE '499 PATENT; IS THAT RIGHT?

A. YES, IT IS.

Q. AND THEN EXHIBIT 2 THAT IS ALREADY IN EVIDENCE, THAT'S THE '712 PATENT; IS THAT RIGHT?

A. YES.

Q. OKAY. NOW, WE'RE GOING TO TALK ABOUT THE CLAIMS IN A MINUTE WHICH ARE FOUND -- SINCE THE LADIES AND GENTLEMEN OF THE JURY NOW HAVE THEIR OWN COPIES, THE CLAIMS ARE FOUND AT THE END OF THE PATENT; IS THAT RIGHT?

A. THAT'S RIGHT.

Q. BUT IN BETWEEN THAT WE HAVE SOMETHING CALLED THE SPECIFICATION; IS THAT CORRECT?

A. YES.

Q. OKAY. SO THE SPECIFICATION OF THE '499 PATENT, EVEN THOUGH THE CLAIMS MAY BE DIFFERENT, ARE THE SPECIFICATIONS OF THE '499 PATENT AND THE '712 PATENT THE SAME?

A. YES, THEY ARE.

Q. SO WE DON'T NEED TO GO BACK AND FORTH BETWEEN THE TWO SPECIFICATIONS WHEN LOOKING FOR THINGS? WE CAN JUST USE ONE SPECIFICATION?

A. THAT'S CORRECT.

Q. ALL RIGHT. LET'S START NOW WITH THE CLAIMS OF THE '499 PATENT.

AND JUST TO ORIENT THE JURY, MR. ANG, COULD YOU PLEASE PUT UP PDX-703.

SO THE '499 -- THE CLAIMS OF THE '499 PATENT, THOSE CAME TO BE IN -- ON FEBRUARY 1ST, 2005, WHEN PHIL DURETTE FILED -- WELL, LET ME BACK UP -- WHEN PHIL DURETTE CANCELLED, IT LOOKS LIKE, TEN CLAIMS THAT WERE PENDING.

IS THAT CORRECT, DR. SECRIST? IS THAT YOUR UNDERSTANDING?

A. YES, IT IS.

Q. AND THEN HE FILED TWO NEW CLAIMS, CLAIMS 53 AND 54?

A. YES.

Q. AND DID THOSE CLAIMS TURN INTO CLAIMS 1 AND 2 OF THE '499 PATENT?

A. YES, THEY DID.

Q. NOW, MR. DURETTE -- OR DR. DURETTE TOLD THE PATENT OFFICE THAT THESE NEW CLAIMS THAT WOULD BECOME CLAIMS 1 AND 2 OF THE '499 PATENT DO NOT -- DID NOT INTRODUCE ANY NEW MATTER INTO THE APPLICATION SINCE, QUOTE, "THEY ARE FULLY SUPPORTED BY APPLICANTS' SPECIFICATION."

BASED ON YOUR EXPERT ANALYSIS, IS THAT STATEMENT TRUE? ARE THEY FULLY SUPPORTED BY THE SPECIFICATION?

A. ABSOLUTELY NOT.

Q. ALL RIGHT. WE WILL GO THROUGH AND WE WILL SEE HOW THEY ARE NOT.

NOW, LET'S GO TO THE '499 PATENT. AND WE'LL GET TO THE '712 IN A MOMENT.

LET'S TURN TO EXHIBIT 1 AND LET'S PUT UP, IF WE COULD, MR. ANG, PDX 704.

SO THIS IS -- AND IF THE LADIES AND GENTLEMEN OF THE JURY WANT TO FIND IT, THEY CAN TURN TO COLUMN 137 OF THE '499 PATENT, AND WE'RE LOOKING HERE AT CLAIM 1; IS THAT RIGHT, DR. SECRIST?

A. YES, IT IS.

Q. NOW, IN READING THIS CLAIM, DID YOU GIVE ANY SPECIAL MEANING TO ANY OF THE TERMS IN THE CLAIM?

A. WELL, BY AND LARGE THE TERMS EXPLAIN THEMSELVES.

THE ONLY ADDITIONS TO THAT WOULD BE THE TWO THAT ARE -- THAT THE COURT HAS GIVEN US CONSTRUCTIONS FOR.

Q. ALL RIGHT. SO LET'S LOOK AT THOSE. DR. STELLA HAD THEM, AT LEAST THE ADMINISTERED PART UP. LET'S GO TO 705.

SO THE COURT, IS IT YOUR UNDERSTANDING, DR. SECRIST, THAT HER HONOR CONSTRUED TWO OF THEM IN A PARTICULAR WAY, COMPOUND AND ADMINISTERING?

A. YES, IT IS MY.

Q. AND WHAT IS THE DEFINITION OF A COMPOUND?

A. A COMPOUND IS A SUBSTANCE THAT CONSISTS OF TWO OR MORE CHEMICAL ELEMENTS IN UNION.

Q. AND WHAT IS THE COURT'S CONSTRUCTION OF THE TERM ADMINISTERING?

A. WE HEARD THIS FROM DR. STELLA, PROVIDING A COMPOUND OF THE INVENTION OR A PRODRUG OF A COMPOUND OF THE INVENTION TO THE INDIVIDUAL IN NEED.

Q. WHEN YOU DID YOUR ANALYSIS IN THIS CASE, DID YOU APPLY THE COURT'S CONSTRUCTION TO THESE TERMS IN THE CLAIMS?

A. YES, I DID.

Q. NOW, DOES THE CONSTRUCTION OF ADMINISTERING IMPACT THE SCOPE OF CLAIM 1?

A. VERY DRAMATICALLY.

Q. IN WHAT WAY?

A. WELL, AGAIN, AS DR. STELLA MENTIONED, IT TAKES A CLAIM THAT ALREADY HAS WELL OVER A MILLION COMPOUNDS AND JUST DRAMATICALLY EXPANDS IT BY ADDING ALL OF THE MULTIPLE OF PRODRUGS THAT HE TALKED ABOUT AS BEING POSSIBLE.

SO IT CONVERTS IT INTO -- I WOULD SAY HE USED THE TERM UNLIMITED MAYBE, OR SOMETHING LIKE THAT.

SO I HAVE TO AGREE WITH HIM. THAT'S WHERE WE ARE ONCE YOU ADD THE PRODRUGS IN TO CLAIM 1.

Q. NOW, LET'S FOCUS ON THE CHEMICAL STRUCTURE OF CLAIM 1. SO IF WE COULD BRING UP PDX 706.

SO WE'RE GOING BACK TO CLAIM 1. NOW, WE'RE GOING TO COME BACK TO THE -- CLAIM 1 IS ACTUALLY A METHOD OF TREATING HEPATITIS C; IS THAT RIGHT?

A. THAT'S CORRECT.

Q. AND WE ALREADY HEARD DR. SEEGER TALKING ABOUT THIS CLAIM

FROM A PERSPECTIVE OF A VIROLOGIST. WERE YOU HERE TO HEAR THAT?

A. YES.

Q. ARE YOU HERE TO TALK ABOUT THE CLAIM AS A MEDICINAL CHEMIST?

A. YES.

Q. AND SO LET'S LEAVE ASIDE FOR A MOMENT THAT IT'S A METHOD OF TREATING HCV AND LET'S JUST LOOK AT THE COMPOUNDS.

SO WE'RE LOOKING AT -- THERE'S TWO STRUCTURAL DRAWINGS HERE. WHAT IS THE TOP ONE?

A. THE -- EXCUSE ME. THE TOP ONE, IF Y, H IS A NUCLEOSIDE, B WOULD BE THE BASE AND Y WOULD BE H, AND THEN THE OTHERS WOULD BE AS DESCRIBED TO THE RIGHT.

THE BOTTOM IS JUST AN EXPANDED DEFINITION OF WHAT B IS GIVEN PICTORIALLY. IT IS A SINGLE RING BASE, A PYRIMIDINE BASE AS DEPICTED WITH R5 AND R6.

SO THERE ARE ONE, TWO, THREE, FOUR, FIVE, SIX, SEVEN -- EIGHT PLACES IN THIS STRUCTURE WHERE YOU COULD PUT IN DIFFERENT SUBSTITUENT GROUPS.

Q. SO IF A COMPOUND -- WELL, LET ME ASK YOU THIS: HOW BROAD IS THIS CLAIM? EVEN THOUGH IT HAS CERTAIN LIMITATIONS, AND WE'RE GOING TO TALK ABOUT THEM IN A MOMENT, HOW MANY COMPOUNDS COULD THIS CLAIM POTENTIALLY COVER?

A. WELL, IF YOU ONLY INCLUDE WHAT IS LISTED ON THIS PAGE, IT IS CERTAINLY WELL OVER A MILLION, AND PROBABLY MILLIONS OF

COMPOUNDS.

IF YOU ADD IN THE COURT'S CONSTRUCTION ON ADMINISTERING, WHICH IS APPROPRIATE FOR THE '499 PATENT, IT BECOMES TENS OF MILLIONS, HUNDREDS OF MILLIONS OF COMPOUNDS BECAUSE YOU COULD DO THIS MASSIVE NUMBER OF PRODRUGS ON THIS SINGLE COMPOUND THAT IS IN HERE, AND AS DR. STELLA SAID, YOU MULTIPLY A MILLION BY A MILLION, WE'RE TALKING ABOUT A LOT OF COMPOUNDS.

Q. AND SO EVEN THOUGH IT COVERS POTENTIALLY MILLIONS OF COMPOUNDS, IF A COMPOUND HAD A DOUBLE RING BASE LIKE MERCK'S MK-608 COMPOUND HAD, DOES THIS CLAIM, EVEN THOUGH IT COVERS MILLIONS OF COMPOUNDS, WOULD THAT COVER A COMPOUND THAT HAD A DOUBLE RING BASE?

A. NO, IT WOULD NOT.

Q. AND WHY IS THAT?

A. WELL, IT ONLY COVERS SINGLE RING BASES, PYRIMIDINE. SO ANYTHING THAT IS A PURINE BASE, A DOUBLE RING BASE, IS NOT GOING TO BE INCLUDED IN THESE CLAIMS.

Q. AND SO LET'S WALK THROUGH SOME OF THE OTHER REQUIREMENTS HERE.

A. OKAY.

Q. AND WHAT WE HAVE A POSITION HERE CALLED R1. SO CAN WE HAVE -- DO WE HAVE ANY GUIDANCE IN THE CLAIM AS TO WHAT ONE CAN PLACE AT R1?

A. YES. R1 IS AT THE C 2' POSITION, IN THE UP POSITION OF C 2', AND IT SHOWS IT AS BEING TRY FLUOROMETHYL C1-4 ALKYL.

SO THE C1-4 ALKYL DESIGNATION, IF YOU TAKE THE TIME TO WRITE UP ALL OF THE POSSIBILITIES, THERE ARE EIGHT POSSIBILITIES.

SO THERE ARE BASICALLY NINE POSSIBILITIES FOR R1.

Q. AND, AGAIN, EVEN THOUGH THERE'S A VAST AMOUNT OF POSSIBILITIES, IF A COMPOUND HAD A HYDROGEN AT THE R1 POSITION, WOULD IT BE COVERED BY THIS CLAIM?

A. DEFINITELY NOT.

Q. NOW, LET'S LOOK AT THE R2 AND R3 POSITIONS. WHAT CAN ONE ATTACH, ACCORDING TO THIS CLAIM, TO THE R2 AND R3? AND YOU CAN BREAK THEM DOWN ANY WAY YOU WOULD LIKE, DOCTOR.

A. OKAY. THANK YOU.

SO I'LL READ WHAT IT SAYS HERE. IT SAYS IN ONE OF R2 AND R3 IS OH OR C1-4 ALKOXY, AND THE OTHER OF R2 AND R3 IS FLUORO.

OKAY. SO THAT MEANS THAT, FOR EXAMPLE, IF R2 IS OH, THEN R3 MUST BE FLUORO.

OR IF R3 IS OH, R2 MUST BE FLUORO.

AND, OF COURSE, YOU CAN DO ALKOXY THE SAME WAY.

THE OTHER THING I WOULD POINT OUT ABOUT THIS STRUCTURE IS THAT YOU CAN SEE THE LINE LEADING TO R3 IS A WAVY LINE. IT'S NOT THE DASHED LINE READING TO R2. IT'S A WAVY LINE.

OKAY. THE WAVY LINE MEANS THAT R3 CAN EITHER BE UP OR DOWN. IT'S DRAWN HERE IN THE DOWN POSITION, BUT IT COULD BE EITHER UP OR DOWN IN THIS STRUCTURE.

SO THAT, AGAIN, ADDS A LOT MORE COMPOUNDS TO THE SCOPE OF

THIS CLAIM BY ADDING IN BOTH OF THOSE.

SO IN THIS -- LOOKING AT R2 AND R3, ONE OF THEM HAS TO BE FLUORO, R2 OR R3, ONE OF THEM HAS TO BE FLUORO.

Q. SO LET'S GO 707, AND WE TRIED TO COLOR CODE WHAT YOU JUST SAID. SO WHAT ARE WE LOOKING AT HERE? WHAT IS THE BLUE AND WHAT IS THE ORANGE AND WHAT IS THE GREEN?

A. SO THE BLUE, R1, THAT WOULD BE ONE OF THE NINE OPTIONS THAT I MENTIONED THAT COULD BE R1.

THE GREEN AND -- I DON'T KNOW WHAT THE COLOR TO CALL THAT. BROWN? ORANGE?

Q. ORANGE I THINK MAYBE.

A. OKAY. ALL RIGHT. GREEN AND ORANGE.

THEN ONE IS OH, ALKOXY, AND THE OTHER IS FLUORO. SO THIS WAY AND THIS WAY, IT HAS TO BE ONE OF THOSE (INDICATING).

SO THOSE ARE THE CHOICES FOR R1, R2, AND R3.

Q. SO WITH THESE LIMITATIONS IN MIND, AGAIN, EVEN THOUGH IT COVERS MILLIONS OF CLAIMS, LET'S SEE IF WE COULD FIND OUR WAY TO THE CLAIMED INVENTION. YOU'RE GOING TO DO A MORE DETAILED DESCRIPTION IN A MOMENT ABOUT THE WRITTEN DESCRIPTION REQUIREMENTS?

A. YES.

Q. BUT IS IT YOUR UNDERSTANDING THAT ONE NEEDS TO LOOK AT THE SPECIFICATION AND SEE IF THE SPECIFICATION KIND OF GUIDES THE -- ONE OF SKILL IN THE ART TO THE CLAIMED INVENTION?

A. IT'S MY UNDERSTANDING THAT THAT MUST BE THE CASE.

Q. AND IN THAT WAY, ONE CAN KNOW WHETHER OR NOT THE INVENTORS WERE ACTUALLY IN POSSESSION OF THE CLAIMED INVENTION BACK WHEN THEY FIRST FILED THE SPECIFICATION IN 2002?

A. THAT'S CORRECT.

Q. OKAY. SO LET'S LOOK --

AND, YOUR HONOR, MAY I APPROACH THE BUTCHER PAPER UP HERE (INDICATING)?

THE COURT: YES.

MS. BROOKS: THANK YOU.

Q. SO WE'LL START WITH THE REQUIREMENTS OF THE ASSERTED CLAIMS. SO WE'RE LOOKING AT THE '499, CLAIM 1. SO I'LL JUST CALL THIS -- SO THESE ARE THE ASSERTED CLAIMS, WHICH IS ALSO THEN KNOWN AS THE CLAIMED INVENTION. IS THAT RIGHT, DR. SECRIST?

A. YES.

Q. OKAY. SO AT THE R1 POSITION, AM I CORRECT THAT BASED ON WHAT WE'RE LOOKING AT HERE, R1 CANNOT -- MUST NOT EQUAL HYDROGEN?

A. THAT'S CORRECT.

Q. AND AT THE BASE IT MUST EQUAL A SINGLE RING?

A. THAT'S CORRECT.

Q. AND I'LL JUST PUT S.R. FOR SINGLE RING.

AND THEN AT THE R2 OR R3 POSITION, YOU MUST HAVE -- AT ONE OF THOSE TWO, YOU MUST HAVE A FLUORO? IS THAT RIGHT, DR. SECRIST?

A. THAT'S CORRECT.

Q. ALL RIGHT. SO THAT IS WHAT IS REQUIRED BY THE ASSERTED CLAIM.

NOW, LET'S GO DOWN HERE AND LET'S LOOK AT THE EXAMPLES THAT ARE IN THE SPECIFICATION.

A. OKAY.

Q. I BELIEVE FROM COLUMNS 40 TO COLUMN 131, THERE ARE 154 EXAMPLES LAID OUT IN THE SPECIFICATION; IS THAT RIGHT?

A. THAT'S CORRECT. THEY'RE NOT ALL CHEMICAL STRUCTURES, BUT, YES, 154 TOTAL EXAMPLES.

Q. OKAY. AND YOU SAID THAT THEY'RE NOT ALL CHEMICAL STRUCTURES. ARE 149 OF THEM CHEMICAL STRUCTURES?

A. YES, 149 ARE CHEMICAL STRUCTURES.

Q. OKAY. SO WE'VE GOT 149 STRUCTURES, AND OF THOSE 149 -- LET'S START WITH THE R1 -- AM I CORRECT -- I'M NOT -- I DIDN'T DO THIS MYSELF. DID YOU DO THIS ANALYSIS, DR. SECRIST?

A. YES, I DID. YES, I DID.

Q. ALL RIGHT. AND OF THE 149 STRUCTURES, ACTUAL STRUCTURES IN THE CLAIM, DO 101 OF THEM, AT THE R1 POSITION, ACTUALLY HAVE A HYDROGEN?

A. THAT'S CORRECT.

MR. GENDERSON: OBJECTION, YOUR HONOR. I HAVEN'T OBJECTED TO LEADING, BUT --

THE COURT: SUSTAINED.

BY MS. BROOKS:

Q. DR. SECRIST, HAVE YOU DONE YOUR OWN ANALYSIS?
A. I DID.
Q. HOW MANY OF THE STRUCTURES IN THE SPECIFICATION HAVE HYDROGEN AT THE R1 SPECIFICATION?
A. 101 OF 149.
Q. AND HOPEFULLY YOU HAVE THIS MEMORIZED, BUT HOW MANY STRUCTURES -- LET'S NOW LOOK AT THE BASE.
A. YES.
Q. HOW MANY STRUCTURES DO NOT HAVE A SINGLE RING AS REQUIRED BY THE CLAIMS, DO NOT HAVE A SINGLE RING AS THE BASE?
A. OUT OF 149 STRUCTURES, 127 OF THEM DO NOT. THEY HAVE A DOUBLE RING.
Q. AND GOING TO THE R2 OR R3 POSITION, HOW MANY OF THOSE STRUCTURES DO NOT HAVE, RATHER THAN HAVE, HOW MANY DO NOT HAVE A FLUORO AT THE R2 OR R3 POSITION?
A. I BELIEVE THE NUMBER IS 135.
Q. SO, DR. SINGER -- SEEGER -- SECRIST.
(LAUGHTER.)
MS. BROOKS: I TRIED THE WHOLE COURTROOM.
THE WITNESS: YOU DIDN'T SAY STELLA. YOU ONLY GOT THREE OF THOSE.
BY MS. BROOKS:
Q. I DID NOT.
DR. SECRIST, LOOKING AT THIS, IF ONE OF SKILL IN THE ART WERE TO FOLLOW THE TEACHINGS IN THE SPECIFICATION, WOULD ONE BE

LED TOWARD THE CLAIMED INVENTION OR WOULD ONE BE LED SOMEWHERE ELSE?

A. WELL, ONE WOULD BE LED CLEARLY AWAY FROM THE INVENTION.

Q. WHY IS THAT?

A. WELL, THE OVERWHELMING MAJORITY OF THE COMPOUNDS HAVE A DOUBLE RING BASE AND NOT A SINGLE RING.

TWO-THIRDS OF THEM, MORE THAN TWO-THIRDS I GUESS HAVE A HYDROGEN UP INSTEAD OF ONE OF THE GROUPS THAT IS WITHIN THE CLAIMS.

AND OVERWHELMINGLY THE COMPOUNDS SIMPLY DO NOT HAVE FLUORINE IN THEM, SO YOU CERTAINLY WOULD BE LED AWAY FROM THE ASSERTED CLAIMS BY THE EXAMPLES.

AND, IN ADDITION, OF COURSE, AS WE KNOW, THE EXAMPLE, THE CLAIMS HAVE -- THE EXAMPLES DO NOT REPRESENT ANY COMPOUNDS THAT ARE WITHIN THE CLAIMS.

Q. NONE WHATSOEVER?

A. NONE. WE'VE HEARD IT BEFORE. I'VE CONFIRMED THAT NONE OF THE EXAMPLES ARE IN THE CLAIMED COMPOUNDS.

Q. HAVE YOU SEEN AN EXAMPLE OF AN ASSERTED CLAIM THAT ONE -- IF ONE FOLLOWED THESE EXAMPLES, THAT ONE WOULD BE LED TOWARD?

A. WELL, WE SAW ONE EARLIER IN THE WEEK FROM DR. SOFIA.

THE PHARMASSET PATENT DOES THAT CERTAINLY.

Q. OH, I -- OKAY. SO YOU'VE SEEN A PATENT --

A. YES.

Q. -- WHERE -- AS AN EXAMPLE OF WHERE ONE WOULD BE LED TO A

PARTICULAR CLAIM?

A. YES, UH-HUH.

Q. WHAT ABOUT -- I'M TALKING ABOUT THIS SPECIFICATION THOUGH.

A. OKAY.

Q. AND WHERE WOULD ONE BE LED IF YOU FOLLOW THE EXAMPLES OF THE SPECIFICATION? WHAT TYPE OF A CLAIM WOULD YOU END UP WITH?

A. WELL, YOU WOULD END UP WITH A DOUBLE RING, A DOUBLE RING BASE THAT DID NOT HAVE A FLUORINE IN IT AND WOULD HAVE OTHER POSSIBLE GROUPS AT 2' OR 3'.

SO IT WOULD -- I GUESS IT WOULD LEAD YOU MAINLY TO THE PREVIOUS PATENT OR THE '395 PATENT. AND, OF COURSE, IN THAT PATENT THESE EXAMPLES, MANY OF THEM, ARE IN THOSE CLAIMS.

Q. LET'S TURN TO CLAIM 2 OF THE '499 PATENT, PDX-708.

NOW, WHAT IS YOUR UNDERSTANDING OF WHAT CLAIM 2 REPRESENTS?

A. WELL, WE HEARD IT EARLIER TODAY, BUT BASICALLY IT ENCOMPASSES EVERYTHING THAT IS IN CLAIM 1. ALL OF THE COMPOUNDS, ALL OF THE PRODRUGS FROM CLAIM 1 CARRY OVER TO CLAIM 2, AND AS WAS SAID EARLIER, IT IS A CLAIM THAT ENCOMPASSES A COMBINATION TREATMENT OF A COMPOUND FROM CLAIM 1 WITH ANOTHER DRUG THAT MIGHT BE OF USE FOR TREATING HCV.

AS WE HEARD FROM DR. MCHUTCHISON AND OTHERS, IT'S -- IN THE ANTI-VIRAL AREA, IT'S OFTEN CRITICAL TO HAVE A COMBINATION OF DRUGS THAT YOU GIVE AS IS THE CASE WITH HIV.

AND THIS CLAIM RELATES TO MAKING SURE THAT THAT IS

COVERED.

Q. NOW, LET'S GO TO THE '712, WHICH IS IN YOUR BINDER AT EXHIBIT 7. THE ASSERTED CLAIMS THAT MERCK IS ASSERTING AGAINST GILEAD ARE CLAIMS 1 THROUGH 3, 5, 7, AND 9 THROUGH 11.

AND JUST TO ORIENT THE JURY, THESE WERE CLAIMS THAT WERE FILED BY A MR. BERGMAN IN 2011 AND 2012? IS THAT YOUR UNDERSTANDING?

A. THAT IS MY UNDERSTANDING. IT'S, IT'S EXHIBIT 2. I THINK YOU SAID 7.

Q. I'M SORRY. EXHIBIT 2. IT SHOULD BE HOPEFULLY IN YOUR BINDER, THE EXHIBIT '712 PATENT?

A. UH-HUH.

Q. AND LET'S PULL UP EXHIBIT 709.

NOW, THESE CLAIMS ARE SLIGHTLY DIFFERENT THAN THE '499 CLAIMS; IS THAT RIGHT?

A. THEY ARE.

Q. AND SPECIFICALLY ARE THEY METHOD OF TREATMENT CLAIMS?

A. NO. THESE ARE COMPOUND CLAIMS, NOT METHOD OF TREATMENT CLAIMS.

Q. BUT IN LOOKING AT THE PATENT, WE'VE SEEN THE ABSTRACT THAT TALKS ABOUT HCV.

SO IS IT -- WHAT IS YOUR UNDERSTANDING OF, EVEN THOUGH THESE ARE METHOD OF TREATMENT CLAIMS, WHAT THE COMPOUNDS ARE SUPPOSED TO BE USEFUL FOR?

A. YES. IN THIS SITUATION WITH A COMPOUND CLAIM, YOU

INDICATE THE COMPOUNDS THAT YOU'RE HOPING TO CLAIM AND A SPECIFIC USE FOR THOSE COMPOUNDS.

SO YOU NEED TO HAVE SOME DATA DEMONSTRATING THE USE OF THOSE COMPOUNDS.

Q. AND WHAT IS THE USE THAT IS DEMONSTRATED, OR AT LEAST CLAIMED TO BE DEMONSTRATED IN THE PATENT?

A. IN THIS CASE IT WOULD BE TO TREAT THE HCV INFECTION.

Q. LET'S GO TO -- OKAY. WE HAVE PDX-709 UP THERE.

WE'RE LOOKING AT CLAIMS 1, 2, AND 3, AND WE SORT OF GROUPED THEM TOGETHER. ARE THERE SIMILARITIES IN THESE CLAIMS?

A. YES. THESE THREE CLAIMS, FIRST OF ALL, ARE VAST NUMBERS OF COMPOUNDS AND I'LL GET TO THAT.

THE ONLY DIFFERENCE BETWEEN THEM IS THE GROUP AT THE 5' POSITION. WE'VE SEEN THIS BEFORE. CLAIM 1 HAS A MONOPHOSPHATE; CLAIM 2 HAS A DIPHOSPHATE; CLAIM 3 HAS A TRIPHOSPHATE.

EVERYTHING ELSE IS IDENTICAL IN THOSE THREE CLAIMS.

Q. AND IS THAT, JUST SO -- I'M GOING TO SEE IF I CAN TAP INTO THIS. SO CLAIM 1, DID I JUST TAP WHERE THE MONOPHOSPHATE IS?

A. CAN I DO THIS?

Q. OH, THAT WOULD BE EVEN BETTER. THANK YOU.

A. ALL RIGHT. SO THERE'S THE MONOPHOSPHATE; THERE'S THE DIPHOSPHATE; AND THERE'S THE TRIPHOSPHATE (INDICATING).

AND I'M DOING THAT WITH MY LEFT FINGER AND I'M RIGHT FINGERED, SO --

Q. THANK YOU, DR. SECRIST.
A. YES.
Q. AND FROM NOW ON I'M GOING TO DEFINITELY LET YOU HAVE CONTROL OF THE MONITOR. AND YOU KNOW YOU CAN CLEAR IT BY JUST CLICKING ON THE BOTTOM LEFT-HAND CORNER WHENEVER YOU WANT TO CLEAR IT.
A. DO YOU WANT ME TO DO THAT?
Q. WHENEVER YOU'RE READY.
A. BOTTOM LEFT-HAND CORNER.
Q. SO BESIDE THOSE THREE DIFFERENCES --
A. YES.
Q. -- MONO, DI, AND TRIPHOSPHATE, OTHER THAN THAT, ARE THE STRUCTURES THE SAME?
A. YES, THEY ARE.
Q. AND CAN YOU DESCRIBE, LOOKING AT THIS, WHAT TYPE OF COMPOUNDS THEY COVER? HOW BROAD OR NARROW ARE THESE CLAIMS?
A. THESE CLAIMS ARE EXTREMELY BROAD. THEY'RE MUCH BROADER THAN THE CLAIMS IN THE '499 PATENT.
AND DO YOU WANT ME TO TALK A LITTLE BIT ABOUT THAT OR --
Q. YES, PLEASE.
A. OKAY. JUST TO POINT OUT SOME DIFFERENCES, IN THE '499 PATENT, THE BASE WAS STILL A SINGLE RING BASE, JUST AS IS THE CASE HERE. BUT IT'S A PYRIMIDINE BASE. BUT YOU CAN SEE HERE IN THE PYRIMIDINE BASE AN E AND AN L THERE.
SO THAT THERE ARE VARIATIONS POSSIBLE ON THE LEFT-HAND

SIDE OF THIS PYRIMIDINE BASES THAT IS PRESENTED THAT WEREN'T INCLUDED IN THE '499 PATENT. SO THAT STILL HAS THE W THAT WE SAW.

AND, OF COURSE, IT IS R6 THERE. AND SO E PRESUMABLY WOULD BE AN R5 AMONG ITS OTHER POSSIBILITIES.

OKAY. SO THAT'S ONE THING.

NOW, IF YOU GO UP TO THE FULL NUCLEOSIDE ON TOP, WE SEE IF YOU REMEMBER THE '499 THERE, R1, R2, R3 ATTACHED TO THE SUGAR RING. THIS HAS THREE MORE THINGS ATTACHED TO THE SUGAR RING. IT HAS AN R4 UP AT WHAT IS THE C 3' POSITION, AND IT HAS AN R12 1 CARBON OVER IT, THE 4' CARBON, AND IT HAS AN R13 AT CARBON 1', WHICH IS THE SAME CARBON THAT HAS THE SINGLE RING BASE ATTACHED TO IT.

SO IT HAS THREE MORE SUBSTITUENTS, EACH OF WHICH CAN BE A VARIETY OF THINGS.

SO IT'S -- IT'S DRAMATICALLY MORE BROAD THAN CLAIM 1 OF THE '499, ALL THREE OF THESE ARE.

Q. HOW MANY COMPOUNDS, IF YOU MADE ALL OF THE VARIOUS SUBSTITUTIONS THAT YOU'RE ALLOWED TO IN THE CLAIM, HOW MANY COMPOUNDS ARE WITHIN THE SCOPE OF CLAIM 1 THROUGH 3 OF THE '712 COMPOUND?

A. EACH OF THEM HAS BILLIONS OF COMPOUNDS AND -- WELL, I'LL JUST LEAVE IT AT THAT. EACH OF THEM HAS BILLIONS OF COMPOUNDS. I WORKED ON THE CALCULATIONS ON MY CALCULATOR UNTIL MY CALCULATOR RAN OUT OF DIGITS.

Q. NOW, DESPITE THE FACT THAT THESE CLAIMS CONTAIN BILLIONS OF COMPOUNDS, IF THE COMPOUND HAD A DOUBLE RING, AS MERCK'S MK-608 DID, IS IT COVERED BY THIS CLAIM?

A. IT IS NOT COVERED BY ANY OF THESE CLAIMS.

Q. LET'S TURN TO CLAIMS 5 AND 7, PDX-710.

SO THIS CLAIM NOW SAID CLAIM 5, THE COMPOUND OF CLAIM 1, WHEREIN B IS, AND IT GOES ON.

AND CLAIM 7 SAYS, THE COMPOUND OF CLAIM 2, WHEREIN B IS.

SO DO YOU HAVE AN UNDERSTANDING OF WHAT THAT MEANS WHEN IT REFERS TO A PREVIOUS CLAIM?

A. YES. IT'S -- IT REFERS YOU BACK TO THE STRUCTURES FROM CLAIM 1 AND CLAIM 2 RESPECTIVELY, BUT IT PINS DOWN THE B TO BE JUST ONE SPECIFIC BASE AND NOT THE GROUP OF BASES THAT WERE INCLUDED IN CLAIMS 1 TO 3.

Q. AND WHAT IS CLAIM 5? WHAT IS THE B?

A. B IN CLAIM 5 IS URACIL. URACIL IS THE BASE THAT IS PART OF URACIL AND SO IT'S CLAIM 5 IS THE BASE.

Q. AND WHAT ABOUT CLAIM 7?

A. CLAIM 7 IS THE IDENTICAL URACIL BASE.

Q. AND NOW LET'S TURN TO PDX-711. THAT'S GOING TO BE CLAIMS 9 THROUGH 11 OF THE '712 PATENT.

AND CAN YOU EXPLAIN TO THE JURY NOW THE DIFFERENCE IN THESE CLAIMS FROM WHAT WE JUST SAW FROM CLAIMS 1 THROUGH 3?

A. YES. THESE THREE CLAIMS ARE DRAMATICALLY NARROW IN FOCUS, DRAMATICALLY NARROW IN FOCUS.

SO YOU CAN SEE NOW WE'RE BACK TO HAVING R1, R2, AND R3 AND B AND Y.

B IS FIXED AS A URACIL RING, AGAIN, IN ALL THREE OF THESE CLAIMS.

AND THEN Y IN ONE CLAIM IS -- IN CLAIM 9 IT'S EITHER A DIPHOSPHATE OR TRIPHOSPHATE, AND IN CLAIM 10 IT SPECIFICALLY CLAIMS THE TRIPHOSPHATE, AND IN CLAIM 11 IT SPECIFICALLY CLAIMS THE DIPHOSPHATE.

NOW, RELATIVE TO R1, R2, AND R3, WHICH WOULD BE IMPORTANT OTHER PLACES FOR THE NARROWING OF THE CLAIMS, IT REDUCES R1 TO JUST BEING C1-4 ALKYL.

SO AS YOU REMEMBER, I TOLD YOU THAT MEANS THAT THERE ARE EIGHT POSSIBILITIES. R2 IS NOW SPECIFICALLY AND ONLY FLUORO.

IF YOU REFER BACK TO CLAIMS 1 THROUGH 3, R2 CAN BE DRAMATICALLY LARGE MATERIALS AND THIS NARROWS IT DOWN TO JUST FLUORO, AND R3 IS EITHER AN OH GROUP OR A HYDROXYL GROUP OR A C1-4 ALKOXY. SO THERE ARE EIGHT OF THOSE.

SO R3 CAN BE NINE DIFFERENT POSSIBILITIES DOWN. AND YOU NOTICE IT'S A WAVY LINE AGAIN, AND SO ALSO THERE ARE NINE POSSIBILITIES UP AT C 3' FOR R3.

BUT THERE ARE NINE POSSIBILITIES WHEREVER R3 GOES. THERE'S ONE POSSIBILITY FOR R2 AND THERE ARE EIGHT POSSIBILITIES FOR R1 NOW.

SO IT'S REALLY DRAMATIC AND NARROW IN ALL THREE OF THESE CLAIMS.

Q. WAS THERE ANYTHING THAT YOU FOUND IN THE SPECIFICATION THAT WOULD HAVE LED YOU TO THIS CLAIMED INVENTION WHERE THERE'S A 2 ALKYL UP AND A 2 FLUORO DOWN, AND AT 3' POSITION AN OH OR AN ALKOXY WITH A NATURAL URACIL BASE, AND AT THE 5' POSITION WITH THE DI OR TRIPHOSPHATE?

A. NO, THERE ISN'T, ABSOLUTELY NOTHING. AND I'VE LOOKED IN GREAT DETAIL THROUGH THE SPECIFICATION MULTIPLE TIMES.

Q. NOW LET'S NOW TURN TO YOUR WRITTEN DESCRIPTION OPINION, DR. SECRIST.

A. YES.

Q. AT PDX-712. WHAT WE HAVE UP HERE IS A DESCRIPTION OF WHAT IT NEEDS, THE PURPOSE OF WRITTEN DESCRIPTION.

WHAT IS YOUR UNDERSTANDING OF WHAT THE WRITTEN DESCRIPTION REQUIREMENT ENTAILS?

A. YES. AT THE TIME THE PATENT IS FILED, THAT WOULD BE IN EARLY 2002, THE INVENTOR MUST BE IN POSSESSION OF THE CLAIMED SUBJECT MATTER. THEY MUST BE IN POSSESSION OF THE CLAIMED SUBJECT MATTER AT THAT TIME IN EARLY 2002.

Q. SO EVEN THOUGH THE CLAIMS WERE NOT FILED UNTIL 2005 AND 2012, THE INVENTORS NEED TO BE IN POSSESSION OF THE CLAIMED INVENTION IN '02?

A. YES, THAT'S MY UNDERSTANDING.

Q. SO DID YOU DO YOUR ANALYSIS THEN FOCUSSING ON 2002?

A. I DID.

Q. AND SO LET'S TURN NOW TO THE '499 PATENT.

A. YES.

Q. LOOKING AT THE CLAIMS OF THE '499 PATENT, AND LOOKING AT THE SPECIFICATION, IN YOUR EXPERT OPINION, WOULD ONE OF SKILL IN THE ART HAVE RECOGNIZED THAT THE PATENT APPLICATION DESCRIBED THE INVENTION AS CLAIMED IN THE '499 PATENT?

A. NO.

Q. WHAT PARTS OF THE PATENT DID YOU LOOK AT TO TRY TO SEE IF YOU WOULD BE GUIDED TO THE CLAIMS OF THE '499?

A. YES. THE SPECIFICATION OF THIS PATENT, IT HAS, I DON'T KNOW HOW MANY, BUT LET'S SAY A DOZEN DIFFERENT STRUCTURES LIKE THE ONE WE HAVE SEEN IN THE CLAIMS.

AND YOU CAN GO THROUGH ALL OF THOSE AND SEE WHAT THEY'RE TALKING ABOUT, BUT IF YOU LOOK AT THE CLAIMS, THEN MAYBE THERE'S SOMETHING TO GUIDE YOU THERE AND THERE'S A ROMAN NUMERAL III BESIDE THE STRUCTURE IN CLAIM 1.

THEN ONE HAS TO PRESUME THEN THAT ONE WOULD NEED TO GO BACK TO FORMULA 3 IN THE SPECIFICATIONS TO SEE IF THERE WAS ANY GUIDANCE TO GET TO FORMULA 3 IN THE CLAIMS.

Q. SO LET'S LOOK AT PDX-713. IS THIS FORMULA 3, SINCE THE CLAIM TALKS ABOUT FORMULA 3, CAN YOU FIND A FORMULA 3 IN THE SPECIFICATION?

A. YES, YES, THERE IS ONE, AND IT'S SHOWN HERE.

Q. AND WHAT KIND OF GUIDANCE, IF ANY, DOES THIS GIVE YOU?

A. WELL, THE FORMULA 3 IN THE SPECIFICATION IS MUCH BIGGER THAN THE FORMULA 3 IN THE CLAIMS.

SO WHAT I WOULD EXPECT AS A PERSON OF ORDINARY SKILL IN THE ART WAS THAT THIS PERSON WOULD GUIDE ME FROM THIS BIGGER GROUP OF COMPOUNDS THAT IS IN FORMULA 3 IN THE SPECIFICATIONS TO STILL A VERY BIG, BUT REDUCED GROUP OF COMPOUNDS WITHIN CLAIM 1.

NOW, IF YOU LOOK FOR THAT GUIDANCE, YOU DON'T FIND IT. SO YOU'RE LOOKING FOR SOME KIND OF A DIRECTION. YOU'RE OUT IN THE FOREST AND YOU'RE LOOKING FOR THE PATH TO GO FROM WHERE YOU ARE TO WHERE YOU NEED TO BE AND THERE'S NO TRAIL THAT GETS YOU FROM ONE SPOT TO ANOTHER HERE AT ALL. THERE ARE NO WORDS THAT HELP YOU IN ANY WAY TO GO FROM FORMULA 3 IN THE SPECIFICATIONS TO FORMULA 3.

Q. NOW, SOME OF THE OTHER CLAIMS REFER TO FORMULAS 7, 8, AND 9. SO LET'S GO TO PDX-714.

AND, FIRST OF ALL, DID YOU FIND THESE FORMULAS IN THE SPECIFICATION?

A. WELL, YOU'RE NOW TALKING ABOUT THE '712 PATENT.

Q. YES, NOW WE'RE GOING TO THE '712.

A. YES, YES. WELL, I LOOKED FOR THESE. AND I THINK WE HAVE SOMETHING TO TALK ABOUT THIS. DON'T WE HAVE DEMONSTRATIVES?

Q. AND SO, IF WE LOOK, THESE REFER US BACK TO FORMULA 1?

A. YEAH, 7, 8 AND 9 HERE SEND US BACK TO FORMULA 1.

Q. ALL RIGHT. LET'S GO TO FORMULA 1 THEN.

SO WE WERE TALKING ABOUT FORMULA 3 IN RELATION TO THE '499?

A. YES.
Q. AND FORMULA 1 NOW IN RELATION TO THE '712. DO WE FIND SOME HELP IN FORMULA 1 IN GETTING TO THE ASSERTED CLAIMS?
A. THE ANSWER IS THE SAME. NO, THERE'S NOT ANY HELP. THERE'S NO GUIDANCE AND NO DIRECTION AND NO PATH TO WALK TO TO GET TO THE ASSERTED CLAIMS FROM THE FORMULA 1 COMPOUNDS IN THE SPECIFICATION.
Q. NOW, MR. GENDERSON IN HIS OPENING STATEMENT REFERRED TO THE SPECIFICATION AS SORT OF LIKE A COOKBOOK, THAT WHILE -- THAT YOU COULD FIND I GUESS THE ULTIMATE RECIPE IN THE COOKBOOK.
DID YOU SEE THAT?
MR. GENDERSON: OBJECTION, YOUR HONOR. I WAS TALKING ABOUT ENABLEMENT, NOT WRITTEN DESCRIPTION.
MS. BROOKS: OH, I APOLOGIZE. I'M SORRY, MR. GENDERSON.
Q. HOLD THAT THOUGHT AND WE'LL GET TO THAT WHEN WE TALK ABOUT ENABLEMENT, DR. SECRIST.
A. OF COURSE.
Q. AND SO LET'S GO BACK AND TALK ABOUT WRITTEN DESCRIPTION. SO YOU FOUND NOTHING IN THE FORMULAS.
WHAT ABOUT THE EXAMPLES? YOU MENTIONED TO THE JURY THAT THERE ARE ACTUAL COMPOUNDS IN THE PATENTS AND, AS I SAID, I THINK THEY START AT COLUMN 30 WITH EXAMPLE 1 AND THEY RUN ALL OF THE WAY THROUGH TO COLUMN 131.

SO DID YOU LOOK AT THE EXAMPLES TO SEE IF THERE WAS ANY GUIDANCE IN THE EXAMPLES THAT WOULD LEAD YOU TO THE CLAIMED INVENTION IN EITHER THE '499 OR THE '712?

A. YES. ACTUALLY, I LOOKED AT THE EXAMPLES FIRST. THEY'RE A MORE FOCUSSED THING TO LOOK AT. ONE WOULD EXPECT THE EXAMPLES TO HAVE SOME EXAMPLES FROM THE CLAIMS THAT ONE COULD LEARN SOMETHING FROM.

SO I LOOKED AT THE EXAMPLES FIRST BEFORE I WENT TO THE MASS OF STRUCTURES WITHIN THE OTHER FORMULAS.

AND, OF COURSE, THERE IS NOTHING IN THOSE STRUCTURES THAT GUIDES ONE TO ANY OF THE ASSERTED CLAIMS IN EITHER PATENT.

Q. IN LOOKING AT THE EXAMPLES, CAN YOU TELL WHETHER OR NOT THE INVENTORS WERE IN POSSESSION OF THE CLAIMED INVENTIONS IN 2002?

A. NO, CERTAINLY YOU CAN'T.

Q. CAN YOU TELL WHETHER -- THIS IS A DOUBLE NEGATIVE -- WHETHER THEY WERE NOT IN POSSESSION?

A. WELL, LOOKING AT THE PATENT, I WOULD SAY THAT THEY WERE NOT IN POSSESSION OF THE COMPOUNDS.

Q. WHY DO YOU SAY THAT?

A. THERE'S NOTHING, ABSOLUTELY NOTHING THAT GUIDES YOU FROM THE SPECIFICATION TO THE ASSERTED CLAIMS, NOTHING, IN EITHER CASE.

Q. AND WERE YOU HERE WHEN A STIPULATION WAS READ TO THE JURY HERE YESTERDAY?

A. I WAS.
Q. AND WHAT IS YOUR UNDERSTANDING OF WHAT THAT STIPULATION MEANS?
A. WELL, I BELIEVED -- DO WE HAVE IT WRITTEN DOWN? OR NO?
THE COURT: WE DO. I CAN SHOW IT TO HIM.
MS. BROOKS: THANK YOU, YOUR HONOR.
Q. SORRY. I SHOULD HAVE HAD THAT FOR YOU, DR. SECRIST.
A. THANK YOU. I WANTED TO GET IT RIGHT.
THIS IS STIPULATION FACT NUMBER 1. NONE OF THE COMPOUNDS DESCRIBED BY STRUCTURE IN THE 154 EXAMPLES IN THE SHARED SPECIFICATION OF THE '499 AND THE '712 PATENTS-IN-SUIT ARE RECITED WITHIN THE ASSERTED CLAIM.
SO THAT'S WHAT I WAS JUST SAYING. THIS STIPULATION MEANS THAT BOTH SIDES AGREE TO THAT FACT.
Q. AND DID YOU DO YOUR OWN INDIVIDUAL ANALYSIS TO CONFIRM THAT WE'RE RIGHT WHEN WE STIPULATED, BOTH MERCK AND GILEAD AGREE THAT THAT'S THE CASE, DID YOU IN YOUR EXPERT OPINION DO A DOUBLE-CHECK?
A. I DID.
Q. AND?
A. AND IT'S CORRECT.
Q. THANK YOU.
YOUR HONOR, I'M ABOUT TO MOVE ON TO ANOTHER SUBJECT MATTER.
THE COURT: THIS IS A GOOD TIME.

ALL RIGHT. LADIES AND GENTLEMEN, WE ARE ENDING EARLY TODAY, SO WE'VE COME TO THE END OF OUR SESSION THIS MORNING.

TOMORROW I'M GOING TO HAVE YOU RETURN AT 9:00 O'CLOCK AND WE WILL AGAIN BE IN SESSION UNTIL NOON.

TOMORROW WHEN YOU LEAVE, I WILL HAVE YOUR SCHEDULE FOR THE FOLLOWING WEEK AND DR. SECRIST WILL JOIN US TOMORROW AT 9:00 O'CLOCK.

SO THANK YOU ALL. LEAVE THOSE BADGES AND ALL OF THE MATERIALS, YOUR NOTES, THE PATENTS, LEAVE ALL OF THAT ON YOUR CHAIRS THERE.

LET ME REMIND YOU YOU'RE NOT TO FORM OR EXPRESS ANY OPINION IN THE CASE OR DO ANY RESEARCH OR INVESTIGATION OR TALK TO ANYONE IN REGARD TO ANYTHING IN THE CASE.

HAVE A GOOD AFTERNOON, AND I'LL SEE YOU TOMORROW MORNING.

(JURY OUT AT 12:03 P.M.)

THE COURT: DR. SECRIST, YOU'RE WELCOME TO GO BACK TO YOUR SEAT.

THE WITNESS: THANK YOU.

THE COURT: ALL RIGHT. WE WILL BREAK FOR THE DAY.

LET ME ASK, AS ALWAYS, ARE THERE ANY HOUSEKEEPING ISSUES FROM EITHER OF THE PARTIES?

MR. GENDERSON: NO, YOUR HONOR.

THE COURT: THANK YOU.

MS. BROOKS: NO, YOUR HONOR.

THE COURT: GOOD. LET ME MENTION A FEW THINGS.

MS. BROOKS: I'M SORRY. APPARENTLY SOMEONE RAISED THEIR HAND AND I DIDN'T SEE THEM.

YOUR HONOR, MAY MR. WARDEN DRESS THE COURT?

THE COURT: YES, OF COURSE.

MR. WARDEN: YOUR HONOR, WE'RE STILL TRYING TO WORK THIS OUT WITH MERCK, BUT WE MAY HAVE AN OBJECTION TO EXHIBITS THAT ARE BEING USED IN THE EXAMINATION OF DR. OLSEN TOMORROW, AND WE'LL BE PREPARED TO PUT THAT IN WRITING BY 5:00 TODAY IF WE CAN'T WORK THAT OUT.

THE COURT: I APPRECIATE THAT. I'LL BE HERE BY 8:30 AND I'LL CHECK MY E-MAIL.

FROM MY PERSPECTIVE -- FIRST OF ALL, MS. BROOKS, DO YOU HAVE AN ESTIMATE WHEN YOU WILL CONCLUDE YOUR CASE IN CHIEF?

MS. BROOKS: WE DO, YOUR HONOR, AND WE ALREADY TOLD MERCK THAT AFTER DR. SECRIST, WE REST.

THE COURT: ALL RIGHT.

SO, MR. GENDERSON, YOU WILL HAVE WITNESSES HERE TOMORROW?

MR. GENDERSON: WE WILL, YOUR HONOR.

THE COURT: EXCELLENT. AND I KNOW IT'S HARD TO PROJECT, BUT DO YOU HAVE -- YOU HAVE THE HOURS YOU HAVE, SO I'M NOT HOLDING YOU TO THIS.

DO YOU HAVE A PROJECTION OF HOW LONG YOUR CASE IN CHIEF WILL TAKE?

MR. GENDERSON: YOUR HONOR, WE WERE HOPING THAT WE WOULD BE ABLE TO, SINCE WE NARROWED OUR CASE, WE WOULD BE ABLE

TO FINISH BY TUESDAY -- WEDNESDAY IN TIME TO DO CLOSINGS WEDNESDAY AFTERNOON.

GIVEN THAT THIS CASE IS GOING ON -- I THOUGHT THIS WAS -- THAT WE WERE GOING TO BE DONE YESTERDAY OR TODAY WITH THEIR CASE. I DON'T, FRANKLY, THINK THAT'S GOING TO BE POSSIBLE.

WE'LL TRY, BUT WE HAVEN'T PUT ON OUR FIRST WITNESS YET AND WE HAVE A NUMBER OF EXPERTS TO RESPOND TO EACH OF THEIR EXPERTS.

AND, FRANKLY, I THINK IT'S PROBABLY GOING TO BE IMPOSSIBLE TO FINISH UNTIL THE END -- BEFORE THE END OF THE DAY WEDNESDAY.

THE COURT: THE END OF THE DAY WEDNESDAY.

MR. GENDERSON: OR EVEN THEN. I CAN'T PROMISE THAT.

THE COURT: AS I SAID, YOU HAVE THE HOURS YOU HAVE.

THEN LET ME JUST SAY, SO THAT YOU CAN HAVE YOUR WITNESSES AVAILABLE, THERE ARE TWO THINGS THAT WE NEED TO DO.

FIRST OF ALL, WE WILL NOT BE IN SESSION ON THE 17TH, NEXT THURSDAY. I'VE SAID THAT BEFORE. YOU SHOULD EXPECT TO BE IN SESSION ALL DAY ON FRIDAY.

I'VE CLEARED -- I'M GOING TO CLEAR AND I'M GOING TO DISAPPOINT THE PARTIES IN ANOTHER CASE THAT WERE HOPING TO DO THEIR CLAIMS CONSTRUCTION HEARING, BUT THEY'LL JUST HAVE TO STEP ASIDE BECAUSE I'M CONCERNED ABOUT FINISHING.

YOU SHOULD ALSO EXPECT THAT WE WILL MOVE DIRECTLY INTO CLOSING ARGUMENT AND SO HAVE THINGS READY.

YOU KNOW, I WOULD LOVE FOR YOU TO REST ON WEDNESDAY SO YOU

HAVE THURSDAY TO COLLECT, BUT I -- YOU KNOW, REALLY THE CLOCK IS RUNNING AND YOU ALL ARE MANAGING YOUR TIME.

AND THE OTHER THING IS THAT I NEED TO HAVE SOME TIME FOR US TO FINISH THE JURY INSTRUCTION DISCUSSION AND LOOK AT THE VERDICT FORM, WHICH WE HAVEN'T DONE.

AND ALTHOUGH I CAN DO THAT ON THURSDAY, THAT -- I THINK THAT WOULD NOT BE WISE BECAUSE YOU MIGHT FINISH SOONER. SO WE WILL NEED TO DO THAT ON MONDAY OR TUESDAY, AND I GUESS WE CAN'T DO IT UNTIL 5:00 O'CLOCK, WHICH DOESN'T MAKE ME TERRIFICALLY HAPPY. I'D RATHER TUESDAY. I HAVE SOMETHING AT 5:00 O'CLOCK ON MONDAY THAT I WOULD LIKE NOT TO HAVE TO MISS.

SO DOES THAT WORK FOR YOU?

MR. GENDERSON: YES, YOUR HONOR.

MS. BROOKS: YES, YOUR HONOR.

THE COURT: AND SO, OF COURSE, I HAVE NOT SEEN THE REVISED SECOND PORTION OF THE JURY INSTRUCTIONS. I DON'T KNOW THAT THERE REMAIN OBJECTIONS, AND OF COURSE I WANT TO GIVE YOU TIME TO MAKE A RECORD AS WE TALKED ABOUT.

BUT IF I COULD KNOW BY MONDAY MORNING FIRST THING WHETHER THERE REMAIN OBJECTIONS ON THE REMAINDER OF THE JURY INSTRUCTIONS, THAT WOULD BE HELPFUL.

AND AS I HAD SAID TO YOU, I WAS INCLINED TO FOLLOW A VERDICT FORM MORE SIMILAR TO WHAT MERCK HAD PROPOSED, AND SO I'D LIKE YOU TO SHIFT TO THAT AND BE PREPARED TO RESPOND AND PERHAPS TO WORK OUT AN AGREED VERDICT FORM.

BUT I AM LOOKING FOR THE JURY TO MAKE DETERMINATIONS CLAIM BY CLAIM, ISSUE BY ISSUE, AND I'M ACTUALLY -- AND SO WE'RE NOT EVEN DEALING WITH DAMAGES, SO YOU WILL DON'T NEED TO GET TO THAT PART, AND WE DON'T NEED TO LOOK AT JURY INSTRUCTIONS ON DAMAGES EITHER. SO THAT REDUCES THINGS A BIT, I THINK.

SO MONDAY I WILL ASK YOU ABOUT ALL OF THIS PROGRESS AGAIN, BUT I -- I WILL BE ABLE TO PUBLISH TO THE JURY -- I MAY PUBLISH TO THEM THAT THEY WILL BE HERE THURSDAY IN CASE THERE'S SOME SWITCH AND THEY'RE ACTUALLY DELIBERATING SO WE DON'T LOSE THE DAY, AND I'LL TELL THEM IT'S A FULL WEEK.

BUT YOU KNOW THAT I'LL LET THEM DELIBERATE, BUT YOU WILL NOT BE PUTTING WITNESSES ON ON THURSDAY NEXT WEEK.

ALL RIGHT. THAT'S EVERYTHING I HAVE. THANK YOU.

YES, MR. GENDERSON.

MR. GENDERSON: YOUR HONOR, ONE OTHER QUESTION.

THE COURT: YES.

MR. GENDERSON: TOMORROW AFTER THE PLAINTIFF'S REST, WE'LL HAVE A MOTION. I ASSUME WE CAN DO THAT ORALLY, BUT OBVIOUSLY WE DON'T WANT TO DO IT IN FRONT OF THE JURY.

THE COURT: WE WILL DEFINITELY DO IT ORALLY, AND USUALLY WHAT WE DO IS THAT YOU SIMPLY MAKE A MOTION AS A PLACE HOLDER, AND THEN AT THE END OF THE DAY YOU ACTUALLY ARGUE IT SO THAT WE CAN GO ON.

AND, YES, ORALLY IS ACCEPTABLE. AND IT MAY TAKE YOU A NUMBER OF MINUTES TO ACTUALLY PUT EVERYTHING ON THE RECORD.

SO I DON'T LIKE TO DO IT WITH THE JURY WAITING, BUT I THINK THE TIMELY PLACEMENT OF THE MOTION, ASSERTION OF THE MOTION IS ALL THAT YOU NEED, AND THEN WE CAN DO IT AT NOON WHEN THE JURY GOES HOME.

MR. GENDERSON: THAT'S FINE.

YOUR HONOR, MAYBE SO WE WON'T DISTURB THE JURY, WE CAN JUST HAND YOU AND I WILL JUST SAY WE MOVE UNDER RULE SUCH AND SUCH AND UNDERSTAND THAT WE WILL ARGUE IT IN THE AFTERNOON.

THE COURT: THAT'S ALL YOU NEED TO DO.

MR. GENDERSON: THAT MIGHT BE EASIER AND THAT WAY WE WON'T HAVE TO DISTURB THE JURY.

THE COURT: THANK YOU. I APPRECIATE THAT. YES.

ALL RIGHT. ANYTHING ELSE?

MR. GENDERSON: I'M SORRY. ONE MORE SECOND, YOUR HONOR.

(DISCUSSION OFF THE RECORD.)

MR. GENDERSON: YOUR HONOR, WE HAD UNDERSTOOD BRIEFING ON DAMAGES AT 5:00 O'CLOCK TOMORROW. DO YOU STILL WANT THAT? OR CAN WE HAVE A LITTLE MORE TIME ON THAT?

THE COURT: I THINK YOU CERTAINLY CAN HAVE SOME TIME ON IT, AND AT THIS MOMENT I DON'T REMEMBER WHAT THE ISSUE WAS. I THINK IT HAD TO DO WITH THE LUMP SUM ISSUE; IS THAT CORRECT?

MS. BROOKS: YES, YES.

THE COURT: ALL RIGHT. YES. YOU KNOW, WE'RE JUST NOT THERE.

AND SO --

MR. GENDERSON: COULD WE HAVE UNTIL MONDAY?

THE COURT: AND, MS. BROOKS, THAT WORKS?

MS. BROOKS: ABSOLUTELY, YOUR HONOR.

THE COURT: ALL RIGHT. MONDAY IS FINE.

ALL RIGHT. GOOD. THANK YOU ALL. I WILL SEE YOU TOMORROW MORNING.

MR. GENDERSON: THANK YOU, YOUR HONOR.

THE CLERK: COURT IS ADJOURNED.

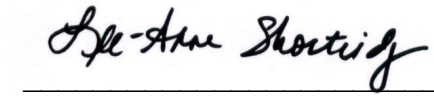
(COURT CONCLUDED AT 12:11 P.M.)

CERTIFICATE OF REPORTERS

WE, THE UNDERSIGNED OFFICIAL COURT REPORTERS OF THE UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF CALIFORNIA, 280 SOUTH FIRST STREET, SAN JOSE, CALIFORNIA, DO HEREBY CERTIFY:

THAT THE FOREGOING TRANSCRIPT, CERTIFICATE INCLUSIVE, IS A CORRECT TRANSCRIPT FROM THE RECORD OF PROCEEDINGS IN THE ABOVE-ENTITLED MATTER.

IRENE RODRIGUEZ, CSR, CRR
CERTIFICATE NUMBER 8076



LEE-ANNE SHORTRIDGE, CSR, CRR
CERTIFICATE NUMBER 9595

DATED: MARCH 10, 2016